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SYSTEMATIC & PRACTICAL

BY

D. J. HAMILTON, M.B., F.R.C.S.E., F.R.S.E.
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COPIOUSLY ILLUSTRATED

VOL. I.

THE UNIVERSITY OF THE NEW YORK HOSPITAL
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TO

SIR JAMES PAGET, BART.
F.R.C.S., D.C.L., LL.D., F.R.S.
VICE-CHANCELLOR, UNIVERSITY OF LONDON,

AND TO

JOHN BURDON SANDERSON, M.D.
F.R.C.P., LL.D., F.R.S.
PROFESSOR OF PHYSIOLOGY, UNIVERSITY OF OXFORD,

THIS WORK IS RESPECTFULLY DEDICATED

BY

THE AUTHOR

PREFACE

THIS work was begun some years since, but owing to my having to devote so much time to the organisation of the duties of my Chair on being appointed to the Professorship of Pathology in Aberdeen University, it unavoidably fell into abeyance for a considerable period. On resuming it, I felt that the system at first adopted was calculated to give too narrow a view of what has now become a very wide and important science; and I accordingly destroyed the early manuscript and remodelled the whole *ab initio*.

It will, I think, be granted that the Pathology of to-day is not delimitable merely as a matter of pure morbid anatomy, pathological histology, pathological physiology, pathological chemistry, or clinical medicine; but that these are simply the members of a great body, and that they are indissolubly bound together. All pathologists of renown, at home and abroad, have served a lengthy apprenticeship in morbid anatomy prior to their becoming exponents of the science of disease. And, for that matter, the continuance in after life of daily observation in the *post-mortem* theatre is as essential to the pathologist as clinical study is to the physician, seeing that it is here that subjects for further inquiry suggest themselves.

A treatise upon the subject of Pathology which is not liberally supported by a basis of morbid anatomy must thus be lacking in thoroughness. It is occasionally asserted that what is seen after death is simply the *result* of disease, and hence can have little bearing upon disease itself. With so short-sighted a view I have no sympathy, for reasons so apparent to any one with the requisite experience as to be unworthy of further discussion.

But morbid anatomy and pathological histology will not carry the earnest inquirer beyond a certain point. In order to arrive at a solution of the great problems of disease, many accessory means of investigation must be adopted. Experiment must be largely resorted to, exact methods of physical research must be drawn upon, animal chemistry must be called in to assist, comparative pathology must contribute largely, and, lastly, the whole record must be controlled by the results of clinical observation.

In constructing this work, I have endeavoured, to the best of my ability, to glean materials from these various sources, and to unite and correlate them to a common purpose. My object has been to present the reader with a living science—a science applicable to the every-day combat with disease.

In order to afford opportunity for considering the subject, both universally and in detail, I have devoted one part to General Pathological Processes, and another to the Special Diseases of each Organ and Tissue.

Pathological technology has become so important nowadays that a text-book must be considered incomplete which does not enter into it at length. It may, perhaps, be judged by some, that more of this has been introduced than was necessary. I have been solicitous, however, to render the book not only serviceable as a systematic guide, but also to make it applicable for use in the laboratory. Two of the chapters on technology have been devoted to Practical Bacteriology, and Systematic Bacteriology will be considered *in extenso* in the second volume.

In every case it will be found that the naked-eye appearances of diseased organs and tissues have been fully described along with those which are microscopic.

All statements of importance from other authors are accompanied by mention of the source from which they have been derived. In order to avoid repetition, and to save space, the works referred to are designated by a number, and a key to the numbers will be found at the end of each volume. In addition to this, a selected bibliography follows each main subject, which may serve to supplement the references given in the text. It must be remembered, nevertheless, that the bibliography does not aim at anything like completeness, but has been compiled more with the view of indicating the landmarks of each subject, and with especial reference to monographs of recent date. Even acting on these lines, want of space has reluctantly compelled me

to omit mention of many excellent treatises, and I must accordingly offer my apologies to their authors for non-insertion.

The Figures have all been drawn by myself from my own preparations, unless where otherwise stated in the List of Illustrations, and my best thanks are due to my publishers for the liberal manner in which they have allowed me to illustrate the book. I am also much indebted to several private individuals and firms for clichés of instruments. Dr. Rohrbeck, of Berlin, has kindly furnished me with most of the woodcuts of bacteriological apparatus.

Finally, I have to return my warmest thanks to the many friends and old pupils who have been good enough to revise the proof-sheets, among whom I must particularly mention my co-examiner Dr. Philip, of Edinburgh, and Dr. Crooke, of Birmingham.

The second volume is in process of preparation, and will be issued with the least possible delay.

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PART I

TECHNICAL

CHAPTER I

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THE SECTIO CADAVERIS

ONE of the first duties of a teacher of any branch of medical science is to call into play and to exercise the observant faculties of his pupils, and no better field for putting these into practice can be found than in the *post-mortem* theatre. With a beginner, it is essential to get into a good system of working and to adhere to this. Such a system can be acquired only after large experience, and accordingly it is an immense help if the teacher can prescribe a certain clear order of procedure. In many of the medical schools of this country and on the Continent, the examination of the *cadaver* is carried out in a very slovenly manner. A few of the most interesting organs are looked at in a hap-hazard sort of fashion; notes are not taken at the time of performance of the *sectio;* and probably after the pathologist has performed six, ten, twelve, or even more examinations in a morning, he vainly sits down to attempt to write out the records, or, it may be, does so a day or two afterwards. Records of this kind are perfectly useless.

In constructing a scientific report, it is necessary, of course, to enter somewhat deeply into detail, and printed forms are recommended in Germany and elsewhere for forensic purposes, so framed as to ensure that no point be neglected in the examination. Some of these forms, such as that employed in Germany, go a little farther than is necessary in this respect, so that they become too complex for every-day use. Very much the same method has occasionally been recommended in teaching clinical medicine, with the effect of rendering the protocol of one case very much like that of all others. On the other hand, some such system is no doubt a valuable safeguard against any grave omission, but it is well to leave a due amount of scope for the discretion and common sense of the operator.

The type of report given in Section 24 is that which the author has found most useful in actual practice, and is the one which he employs at the present day. It is very simple, and can be easily

written out in an ordinary note-book before commencing the examination. It is much more convenient, however, to have it printed, leaving spaces of appropriate size between the different headings.

1. **Instruments.** *Knives.*—Four kinds of knife are desirable: (*a*) a sectio knife for opening the body; (*b*) ordinary dissecting-room scalpels; (*c*) a long knife for opening the orifices of the heart and for cutting into the brain; and (*d*) a curved probe-pointed bistoury.

There is no doubt that what Virchow (No. 1) says in regard to the kind of knife to be used for the actual opening of the body and removal of organs is correct, and that the usual knives provided for the purpose are, as a rule, unsuitable. It ought to be made on the principle of a butcher's knife, that is to say, it should be large, have a deep belly, and end in a somewhat obtusely acuminated point. The blade should be firmly set in the handle, and the latter be so large that it can be held in the whole hand. The larger the knife the quicker will the examination be made, and the more clearly will the organs be excised. In every *post-mortem* case there ought to be at least three such knives, and in a large hospital six or more should be provided.

FIG. 1.—SECTIO KNIFE FOR ORDINARY *Post-Mortem* WORK.

The long knife for opening the valves of the heart and for cuting into the brain should have a blade at least 10 inches long and $\frac{3}{8}$ths of an inch broad. An ordinary amputation knife will not do. It must have a rounded blunt extremity, so that on introducing it through the orifice of the aorta or pulmonary artery it does not catch upon the cusps of the valve and wound these. Even for incising the brain there is no occasion for a point.

The curved probe-pointed bistoury is for the purpose of cutting through the dura mater in removing the brain.

Dissecting Forceps.—Two or three pairs of various sizes.

Bone Forceps.—One very large pair, in fact the largest bone forceps made, with very rigid handles, which ought to be roughened, so as to get a firm grasp. A smaller pair may be added.

Scissors.—A fine-pointed pair; two larger sized, made broader and stronger; and a pair of intestine scissors with a hook at the end.

Saw.—One is sufficient for most purposes, but it ought to be very strong, and the teeth particularly well set. The back should be movable, and the blade not less than eleven inches long. The saw provided in most cases is far too short. A small saw may be conveniently added, suitable for removing small bones, such as those of the ear.

Chisel and Mallet.—The former ought to have a straight, not the

usual curved, edge, and if it is provided with a cross handle, this ought to be fixed and made rough and broad on the surface, so that the mallet does not slip when applied to it. The mallet is to be made of heavy wood.

A Hook for removing the calvaria. A very useful instrument for slipping into the incision in the skull instead of the very dangerous practice of inserting one's fingers. It should have a strong cross handle. It is particularly serviceable in medico-legal examinations where the employment of a mallet is unjustifiable.

Three Flat Strong Needles for stitching up the body.

A Set of Graduated Cones, such as are employed in measuring apertures of different kinds, divided into fractions of an inch. These are by far the best instruments for measuring orifices.

FIG. 2.—GRADUATED CONES USED FOR MEASURING ORIFICES.

A Set of Glass or Wedgwood Measures for liquids.

A Gallon Measure made of metal.

A Balance with a hollow scale capable of holding a large-sized liver or lung.

Two Injecting Syringes and Nozzles.—The large one should be from 8 to 10 oz. capacity; the small, from 3 to 4 oz.

A No. 8 Silver Catheter.

Several Silver Probes and a Blow-pipe.

Three Hooks attached by a chain, for dissecting purposes. Two sets.

A Hartnack Microscope, with objectives Nos. 3 and 7, and ocular No. 3; and slides, covers, and needles (see Sect. 53).

An Ether Freezing Microtome and Knife.—Too expensive an instrument should not be purchased, as it is preferable to employ ice for the freezing of most tissues, unless of course where this cannot readily be procured. The ether freezing microtome is advantageous in the *post-mortem* room because of the readiness with which a small piece of tissue can be frozen and cut. That recommended by Dr. Lewis,

or the later one invented by Dr. Cathcart, is sufficient for all practical purposes, and both are very cheap (see Sect. 39).

A Double-bladed or Valentin's Knife.—Before the time of freezing microtomes this instrument was in great requisition for making a comparatively thin and large section. It affords a rough view of the histological characters of a tissue, but is not to be compared in efficiency with a freezing microtome. The parallel blades are so adjusted that by means of a fine screw they can be approximated to any required distance, and fixed in that position. The knife is then passed through the organ with a sawing motion, and the section comes out between the blades. The section, however, although occasionally successful, is apt to be torn and to be of unequal thickness, so that, in later times, this instrument has fallen into disuse.

A Small Narrow Wooden Foot-rule graduated for inches on one side and centimètres on the other.

A Measuring Tape similarly graduated.

2. **Reagents.**—(*a*) A solution of equal parts of Liquor Iodi (P.B.), and water; (*b*) a large quantity of $\frac{3}{4}$ per cent. solution of common salt; (*c*) a 1 to 20 solution of carbolic acid in water, for disinfecting the hands after an examination.

3. **External Appearances.**—If there is one rule more important than another in making a *post-mortem* inspection, it is perhaps *to examine the exterior of the cadaver before proceeding to the interior.* Unless this is attended to, it will be found impossible afterwards to ascertain certain facts which may be of the greatest value in the report. One can never be too particular in taking note of what may even seem extraneous and unimportant appearances on the outside of the body, as these often come to have a peculiarly direct bearing upon the case. Every medical jurist must have had some remarkable experience of the truth of this in cases where the body has remained unidentified after death; but, in all cases, everything abnormal in the external appearances should be noted before the body has been touched with the knife.

The *cadaver* should be *weighed*, if this is practicable, and the *height* and *girth* at the shoulders noted. It is a good rule to record next the state of the body in regard to *general nourishment*, the extent of the *rigor mortis*, and the amount of *post-* or *ante-mortem lividity.* In describing the lividity employ the terms "slight," "medium in amount," or "great," on dependent parts, upper surface, tips of the ears, or fingers, etc., as the case may be. On no account omit to *turn over the body* in order to examine the back. It is here, of course, that the *post-mortem* lividity is usually greatest, and while taking note of this, any other abnormalities should be observed, although they need not necessarily be described along with the lividity. Examine next every part of the surface in detail, from the crown of the head downwards. The *scalp* should be gone over with the hands in order to detect the presence of any wound or excrescence upon it; and the

quantity and colour of the *hair* on the scalp, eyebrows, and eyelashes, etc., should be taken into account. Then the state of the *pupils* and *cornea*, the *liquid exuding from the mouth or nostrils*, and the condition of the *lips* and *ears* should be examined in regular rotation. The *neck*, *chest*, *abdomen*, *genital organs*, *groins*, and *limbs* are each to be carefully scanned, and various parts tested by pressure for œdema. If a localised livid patch is suspected to be a bruise, incise it and see whether blood has been effused into the tissues.

4. **The first Incision** runs from the sterno-clavicular articulation down to the symphysis pubis, and should be made in one sweep with the large sectio knife previously described, the head of the *cadaver* being to the operator's left hand. As much as possible of the belly of the knife should be pressed against the tissues in doing this, so that a free and continuous incision is made through the skin and subcutaneous fat. Care, however, must be taken not to go deeper than this in passing over the abdomen, otherwise the stomach or other abdominal viscus may be wounded. The abdomen should now be opened by an incision in the epigastrium sufficiently large to admit two fingers. The fingers of the left hand are introduced into the wound and traction is exerted by them upon the abdominal parietes so as to pull the latter away from the underlying coils of the intestine. With one sweep the incision into the abdomen can be carried down to the symphysis pubis, and in making this deep as well as the primary superficial wound, the umbilicus should be avoided. *Note the condition of the abdominal organs*, as exposed by the opening in the wall, *before they have become disturbed*. The position of the diaphragm in newly born children is of importance, and should be examined immediately on opening the abdominal cavity, and before any wound is made into the chest.

Measure all liquids found in any part of the body, and on no account make a random guess at their quantity. Any further description of these liquids may be appended to the statement of the actual quantity, as, for instance, "and the liquid distended the pleural cavity, compressing the lung to half its bulk," but the actual quantity should always be mentioned. In removing ascitic liquid it is best to squeeze as much out as possible through the small incision in the epigastrium, continuing to do so as the incision in the abdominal wall is enlarged.

If a perforation of the intestine is suspected, or if there be an abdominal tumour, examine the position of these with as little disturbance of the abdominal viscera as possible. If after death the stomach has become digested, and the contents have escaped into the abdomen, notice where the effused contents lie. In an *ante-mortem* perforation of the gastro-intestinal tract the contents are usually diffused more or less throughout the abdominal cavity. In one which has occurred *post-mortem*, the half-digested food lies around the perforation.

The soft tissues are now to be removed from the chest wall with the large sectio knife, and, in doing so, a constant drag should be kept

upon them with the left hand, while a number of *long* incisions are made with the knife. The abdominal muscles should be entirely severed from the lower border of the ribs, and the ribs freely exposed for some distance beyond the cartilages.

The Cartilages, if uncalcified, are to be divided with the ordinary sectio knife, and this should be done in a slanting direction; they are thus much more easily cut. If they are calcified it will be necessary to employ the saw. The left corner of the sternum and its attached cartilages is then to be lifted up, and the diaphragm and other muscles detached from it, the same being done on the opposite side. The remainder of the sternum is now to be detached from underlying connections, care being taken not to injure the pericardium. It is well to introduce the hand under the sternum and to feel whether there be any aneurism or other tumour attached to it, so as to prevent injuring this by the careless use of the knife. The clavicular attachment of the sternum should not be separated, but the sternum is to be sawn through a short distance below it. If the clavicles are detached from the sternum there is difficulty in afterwards filling up the ugly gap which is left, the weight of the upper extremities tending to separate the clavicles. Do not divide the periosteum of the anterior aspect of the sternum for it acts as a hinge in supporting the bone after the body has been closed.

Leaving the abdomen for the present, the *cavities* should be systematically explored—firstly for liquids, and secondly for adhesions or other abnormalities upon their surfaces. Do not open the pericardium before this has been done, as the liquids of the two cavities may get mixed, so rendering it impossible to measure them. The thoracic organs have now to be examined in the following order.

5. **The Heart.**—If the pericardial sac contains much liquid, in addition to recording the quantity of this, take the greatest measurements from base to apex and transversely before it has been opened. Observe how much of the sac is covered by the lungs anteriorly, and after having noticed any other abnormalities in connection with its outer surface, *open the sac* in the following manner. Two incisions are made, the one running along the diaphragmatic border, the other along the margin of the right lung. In this manner a V shaped flap of pericardium is detached which ought to be held back by an assistant while the operator collects the pericardial liquid. This is done by pulling up the apex and allowing the liquid to gravitate to the lowest part of the sac. The liquid can then be readily withdrawn without any of it being lost.

The heart is next replaced and the organ *examined in situ*. Measure it from base to apex and at its greatest transverse diameter, and having done so, see whether it is displaced in any way, whether there is any fibrinous effusion upon the interior of the pericardial sac, or adhesions between its surfaces. Note the position of the apex in relation to the ribs and the mammary line. Next *examine the state of the cavities* as

regards the contraction or relaxation of their walls and the amount of blood contained within them. In most cases it is unnecessary to measure the *amount* of blood, and in all cases where the blood is fluid such measurement must necessarily be fallacious, from the fact that the blood readily flows from one cavity into another after death, and from the large vessels back into the heart whenever the latter is opened. Hence in most cases a more useful method is simply to state that the chamber in question "contained a little blood," "was almost empty," "was half-filled," or "was distended with blood," or some such similar expression indicative of the relationship of the actual quantity of blood to the organ. For, after all, the actual quantity gives very little information if taken alone, seeing that the size of the chambers differs so much in different subjects. It may, however, be better in medico-legal cases to err on the safe side by measuring the actual quantity in the left and right chambers in addition to stating the relationship of this quantity to the walls. In cases of death by drowning and other forms of asphyxia, as well as in death from cardiac syncope, profuse hæmorrhage, etc., it is also advisable to do so, but in the majority of ordinary cases it is sufficient merely to state the amount of distension present in the four chambers and large blood-vessels.

Having done this, *make an incision* about one inch long *into the pulmonary artery* some distance beyond the valve, and introduce the forefinger down to the bifurcation of the vessel.[1] Notice whether there is any clot contained in it, and ascertain from its appearance whether such be *ante-mortem* or *post-mortem*, and whether it be locally produced or detached from some large vessel. The incisions, where the organ is opened *in situ*, should be the same as those about to be described, but where it is unnecessary to measure the actual amount of blood, or to retain it for purposes of analysis, it is not advisable to open the heart until it is removed from the body.

Remove it by cutting through the vessels as far away from the organ as possible. Begin with the vena cava inferior; sever the connections of the pulmonary vessels next, and, lastly, cut through the aorta and vena cava superior. In dividing the aorta, draw the heart up on the reflected sternum so as to pull it out of the chest as far as possible. *Then follows the more detailed examination of the surface and chambers.*

Its Surface.—Under this are to be noted the condition of the epicardium and the sub-epicardial fat. In cases of general obesity the sub-epicardial fat is usually much increased in quantity. Thickenings of the epicardium from friction or "milk-spots" are most common on the surface of the right ventricle anteriorly and posteriorly and at the apex. In acute pericarditis the epicardium becomes roughened from a coating of fibrinous lymph, so that the surface should be carefully

[1] The author remembers once finding a thrombus which had been detached from a varicose ovarian vein firmly fixed at the point of bifurcation. The thrombus corresponded in shape to one of the veins, it was of old formation, and the symptoms pointed to its having become suddenly impacted.

inspected to make sure that it retains its natural glossiness. Caseous tubercles are rarely found on the surface of the pericardium; for some unexplained reason it is, of all the serous membranes, the least frequently affected with tuberculosis. The condition of the *coronary arteries* should be examined in all cases. Rupture of the heart by no means infrequently happens from fatty degeneration caused by calci-

FIG. 3.—METHOD OF OPENING THE LEFT VENTRICLE.

The dotted line *a* represents the measurement of one inch below the left border of the base of the pulmonary artery, while the dotted line *b* represents the half-inch to the left side of this. The point of the knife is entered at the extremity of the latter, and is drawn downwards in the direction of line *c*, *c*.

fication of the coronary arteries following upon atheromatous endo-arteriitis. The muscular fibre becomes fatty, softens, and under some unusual strain gives way, the escape of blood in most cases causing almost immediate death.

Slit the coronary vessels open with a probe-pointed bistoury. If they are healthy they should have a bluish-pink tint and be quite smooth. Any other features of note on the surface should all be diligently recorded, such as an unusual size of either of the ventricles, etc.

The Interior.—The primary openings into the ventricles should be made without injuring the valves, and without interfering with the septum. Many methods are recommended for opening the heart, but the author has found the following most serviceable:—

Lay the heart on a flat surface with its posterior aspect downwards. The best guide to the various aspects of the heart is the pulmonary artery. Seek for this first; its position will at once indicate the anterior aspect of the organ. Lay the organ, therefore, with its posterior aspect in contact with the table, the apex pointing towards the operator. Introduce the point of the ordinary sectio knife one inch below (Fig. 3, *a*), and half an inch to the left side (*b*) of the left border of the pulmonary artery at its base. The exact point of course varies with the size of the organ, and a little allowance must be made for this, but the above generally fixes the point of entrance sufficiently well. Push the knife backwards and a little downwards until it passes into the opposite wall of the ventricle. Then draw it downwards and very slightly outwards (*c*, *c*), and the left ventricle will be opened. A flap is thus made sufficiently large to remove the blood and to test the competency of the aortic valve.

The next step is to *test the competency of the aortic valve* by allowing water to run into the aorta. Do not make the mistake of testing the valve before opening the ventricle. In order to get the cusps of the valve to close, the heart must be suspended by grasping the cut edge of the aorta; and it is essential to suspend it merely by the ascending aorta, otherwise, almost to a certainty, the valve will be rendered incompetent. Allow a fairly powerful stream of water to run in, and if the valve is competent the water ought to be retained. Be careful to look into the aorta to see that the cusps meet, and, of course, remove any clot which may be present in the aperture.

Testing with Air.—The above is the usual means employed for testing the competency of the valves. It is, however, faulty from being applicable only to the aortic and pulmonary artery orifices, as well as from the pressure exerted by the water on the valves being considerably less than that of the blood during life. It, moreover, does not display the valve in motion, and hence fails to show what the mechanism of a particular incompetency may have been.

The substitution of air for water will be found to be a great improvement on the water method, as it may be utilised for all the valves, and can be made to display the action of the cusps in motion. The following is the manner of adapting it to the various orifices:—

An incision is first made into the left auricle, and any *post-mortem* clots are carefully removed from the left chambers through it. Another incision large enough to admit the nozzle of a half-inch tube is made into the ventricle near its apex and in the line of that required for laying it fully open. The tube is joined to a bellows, and air is driven intermittently into the ventricle by means of it, the aorta having been meanwhile closed. The valve will be seen to

and close, according as the air is aspirated or driven out of the bellows. A like procedure is adopted for the demonstration of the tricuspid.

To test the aortic valve, the incision before described as necessary to lay open the left ventricle is continued up as close to the valve as possible without injuring it. The tube is tied into the aorta, and the action of the valve is watched from below. The same method is used to test the competency of the pulmonary artery valve.

As a matter of fact the tricuspid, in the human heart, will always be found more or less incompetent.

Open the right ventricle in the following way:—Lay the organ on the table with the left ventricle (Fig. 4) lowest and the apex pointing to the right of the operator. Grasp the thin wall of the right ventricle between the fingers and palm of the hand, so as to make sure that

FIG. 4.—METHOD OF OPENING THE RIGHT VENTRICLE.

it is separated from the septum. The wall of the right ventricle is usually so thin that the position of the septum can be readily felt. With the long brain knife cut a V-shaped flap in the ventricle from the apex upwards. The size of this should be such that free access is gained to the cavity, but not so extensive as to injure the tricuspid valve. The incision can be made without danger of injuring any parts of importance, if the ventricle is thoroughly gathered up by the fingers from the septum. Test the competency of the pulmonary artery valve by the same method as that employed for the aorta.

Return to the left side of the organ and measure the diameters of the orifices with the cones depicted in Fig. 2. Take the measurement of the orifices in the following order:—Aorta, mitral, pulmonary artery, and tricuspid. Several points require to be remembered in using these cones, namely—(1) Push them through in the same direction as that in

which the blood runs. (2) Be particularly careful not to detach any vegetations adhering to the cusps. (3) Do not use any force, but simply run the cone into the orifice until it is felt to catch; of course, if force is employed the apertures may be stretched with an instrument of this kind much above their real size.

(For size of the various orifices, see Diseases of Heart).

This method of measuring by cones is by far the most convenient. Under no circumstances should the operator's fingers be taken as the gauge. The range in size of different pathologists' fingers is so extensive that the method, although still followed in many German schools, is totally unscientific and worthless as a standard of measurement. The diameters are read off by means of the cones in a few seconds, and having once got the measurements in inches or centimètres, it is quite unnecessary to indulge in those vaguest of all terms "large" and "small." In order to introduce the cones into the mitral and tricuspid it is necessary to open each auricle. An opening sufficiently large for the purpose may be made between two of the veins in the case of the left, and between the two venæ cavæ in that of the right. The incisions can readily be stitched if it is desired to retain the organ as a museum specimen.

Open the aortic valve in such a way that the incision cuts through the division between two cusps. Virchow (No. 1) recommends the use of scissors for this purpose, but if certain precautions be attended to, an even better instrument is the long brain knife. This knife is made round at the point purposely to avoid catching the cusps, and in the case of the aorta, the division between two cusps will always be hit (unless the valve is seriously deformed) if the following procedure be adopted:—*Pass the knife into the aorta from below upwards, and cut through the valve and ascending portion of the arch by keeping the edge playing as closely as possible upon the pulmonary artery.* As the pulmonary artery is considerably curved, the knife is directed, supposing the heart to be in the body, inwards, upwards, and outwards. The organ should be loosely held in the left hand, and the closer the knife turns round the curve of the pulmonary artery the more cleanly will the incision run through the interval between two cusps. Such an interval always lies close upon the pulmonary artery, and it is this which it is desired to strike. If the operation has been properly performed, the pulmonary artery should not be injured, but the knife should have run in the cellular tissue between this vessel and the aorta. If the valve is very much distorted by disease it is better to continue the primary incision into the ventricle close up to the base of the aortic valve, and then noticing where the interval between two cusps exists, to divide with the long knife or scissors.

Examine the interior of the left side before proceeding to the right. It is a good rule to begin with the aorta, coming down to the aortic valve, the interval between the aortic and mitral, the mitral itself, and the endocardium generally. Note, lastly, the size of the cavity of the ventricle and thickness of the wall, along with any disease of the muscular fibre. Grasp the bases of the aortic cusps and notice whether

they are unusually indurated and cartilage like. Examine the edge of the mitral with a similar purpose.

In examining the mitral, the operator should not forget to look into the valve from the left auricle. It is in this way that the best view is obtained of a contracted mitral, and frequently a crop of vegetations will thus be discovered which otherwise might be passed over unheeded.

Measure the size of the ventricular cavity from the base of the aortic cusps down to its apex, and *measure also the thickness of the wall* at its thickest and at its thinnest parts.

This method of measuring the ventricle is faulty in many respects, but will be found to give a fairly accurate idea of any enlargement or diminution in size. A small foot-rule is the best means of measuring both it and the thickness of the wall. The measurement in inches may be supplemented by a description of the appearance of the cavity—as to whether it bulged more in one part than in another, or as to its general capacity. Taken together the two methods will give a very fair idea of its condition. Remember, however, that the size of the cavity, especially a very small cavity, depends in part upon whether the heart has died in a state of systole or not, and may not necessarily be an index of disease. An unusually large cavity is always the result of disease.

We have now finished the examination of the whole of the left side, unless the auricle, and this ought next to be described as to capacity and anything else that may be found amiss with it. Unfortunately there is no ready means of judging of the capacity of the auricle, and hence all will depend on the operator's experience.

The right side of the heart has as yet been opened only by the V-shaped primary incision. In order to see the interior of the ventricle properly, as well as the state of the valves, it is necessary to extend this incision through the pulmonary artery orifice. The orifices on this side have already been measured along with those of the left, a precaution that is necessary in case the pulmonary artery should be wounded in opening the aorta. How can the pulmonary artery orifice be opened so as to cut between two cusps? The rule is very simple: *Holding the heart in the left hand, cut as close on the ventricular septum as possible.* The knife is pushed through the orifice from below, its edge is turned towards the septum, and it is then cut out, care being taken, of course, that the septum is not injured in dividing the valve. In this way, as in the case of the left side of the heart, the incision into the valve is connected with that which was primarily made into the ventricle, and so a continuous flap of tissue can be thrown back. This method of opening the pulmonary orifice is moreover the best to employ for the purpose of showing the interior of the organ as a museum specimen.

When the right side is thus laid open, begin the description of its interior with the pulmonary artery, and proceed downwards. Measure the length of the ventricle from the base of the cusps of the pulmonary artery to the apex of the cavity, and, likewise, the thickness

of the wall at its thickest and thinnest parts. The right ventricle is usually a little larger than the left (see Diseases of Heart).

Lastly, *examine the auricle*, and *weigh the organ;* and the description is completed so far as naked-eye features are concerned. Remember that the heart, unlike other organs, must not be weighed at the commencement of the examination. The blood-clot which it usually contains would vitiate the result.

Microscopic examination of the fibre must be made in all cases where it seems to be abnormal ; and in cases of sudden death, especially in cases which are the subject of a medico-legal inquiry, it is safe, even where the tissue seems quite healthy, to do so as well. Those inexperienced in the microscopic examination of the heart fibre, however, should be very careful in drawing conclusions from microscopic examination alone if the fibre does not seem to be altered to the naked eye. This should specially be remembered where death is supposed to have been due to fatty degeneration of the heart. True fatty degeneration of the heart is, contrary to what is popularly supposed, a rare disease. In the healthiest heart fibre an occasional oil globule may be detected, and a deposit of pigment which occurs in nearly every adult heart, or a granularity from precipitation of the albumin of the fibre, is frequently mistaken for fatty degeneration. None of these has any great lethal importance, and all are incapable of being detected with the naked eye. When fatty degeneration does occur, of such magnitude as to cause a fatal result, it shows, with unaided vision, an unmistakable and characteristic appearance.

The subject is fully discussed under DISEASES OF THE HEART.

CHAPTER II

THE SECTIO CADAVERIS—(*Continued*)

6. **The Lungs.**—These are to be examined after the heart. Cut out the left one first, and if adhesions exist between the pleuræ, separate these by tearing and cutting. Begin at the apex and pull downwards. When a bilateral organ is excised, such as the lung, the left one should be laid on the table to the left of the subject, and the right to the right. It is well also to remove the *left* organs first. Weigh each before it is touched with the knife. Examine the surface with the utmost care, and afterwards cut into the organ by one large incision from apex to base. Make a series of parallel incisions, but in none of them carry the knife so deep as to completely sever the parts. Commence the description of the interior of the organ at the apex.

7. **The Liver.**—Having finished the examination of the heart and lungs we come back to the abdomen, and the first organ to be removed here is the liver. In removing it, incise the left half of the diaphragm as far back as the spine, and detach the organ from the under surface of the diaphragm by cutting through the falciform ligament. Introduce the left hand behind the right lobe, and push the whole organ out of the body and to the right side, until it comes to hang over the ribs. Then sever with the knife the attachments to the stomach and neighbouring parts as well as the bile duct and vessels. In cases of jaundice, or where the bile duct is suspected to be occluded or altered in any way, first examine the parts *in situ* and afterwards remove the organ with the duodenum and the opening of the common duct *en masse*. By squeezing the gall bladder, the bile may be made to run through the duct into the bowel if no obstruction exist. In squeezing out the bile from the gall bladder, catch the whole viscus in the palm of the hand and compress it equally throughout, otherwise it is sometimes difficult to make the bile flow. Examine the colour of the bile and slit up the gall bladder. Weigh the organ and record everything of note on the surface before going to the interior. Open it by a series of cuts from side to side,

and note the amount of blood that escapes. Wash the cut surfaces, and proceed to their examination.

8. **The Spleen** should now be removed. Its vessels and other attachments should be cut, not torn, and a single incision in its long axis will usually be sufficient to expose its condition. Like other organs, it should be weighed immediately after removal from the body.

9. **The Kidneys** come next in order, the left first. Remove them by making a large cut into the lumbar peritoneum. Pass the hand behind the organ, and separate the surrounding cellular tissue. Remove the suprarenal capsule with the kidney. It can be readily detached after the organ has been got out, while, if left in the abdomen, it is apt to be injured or lost. Separate the surrounding cellular tissue and fat from the kidney, and weigh it. Open by a single long incision from end to end through the convex border, carrying the incision so far through the kidney substance that the medullary pyramids are completely severed, the only attachment remaining between the two halves being the tissue of the pelvis. If a partial incision is made, the organ can never be properly examined. Strip off the capsule on one side either partially or completely. It is usually unnecessary to strip it off on both sides, and it is advisable to leave one side attached for future microscopic examination. Observe the shape, size, and consistence of the organ, and the extent to which the capsule is adherent in the denuded half. Examine the surface, its colour markings, and amount of congestion, noting particularly whether it is granular or smooth, or whether there are cysts upon it. The stellate venous radicles on the surface sometimes become very apparent from congestion.

Having finished the surface, come to the interior, and observe, firstly, if there is any marked disproportion in size between the cortex and medulla. If a straight line be drawn from the surface of the organ to the apex of a pyramid through the cortex and medulla, when the kidney is laid open as above described, the medulla will be found, supposing the kidney to be healthy, to occupy three parts of the line, the cortex one. In other words, the medulla is proportionally three times as large as the cortex; and this prevails not only in the adult, but also in the child. Of course it must be remembered that the boundary of the cortex where it abuts upon the medulla is not represented by a single uninterrupted curve, but that a portion of the former dips down between each two medullary cones. The cortex is in reality a cap like the pileus of a fungus. It often happens, consequently, that in large microscopic preparations a piece of the cortex is found lying collaterally with the bundles of straight tubes. What is referred to above is the proportional size of the cortex and medulla from the apex of a cone to the surface of the organ. It forms a very fair means of gauging any alteration in size. As the actual thickness of the cortex and medulla varies so much in different individuals, it is of little use taking the measurements in fractions of an inch. The *relative* size of the one to the other is of much more importance, and can

inspected to make sure that it retains its natural glossiness. Caseous tubercles are rarely found on the surface of the pericardium; for some unexplained reason it is, of all the serous membranes, the least frequently affected with tuberculosis. The condition of the *coronary arteries* should be examined in all cases. Rupture of the heart by no means infrequently happens from fatty degeneration caused by calci-

FIG. 3.—METHOD OF OPENING THE LEFT VENTRICLE.

The dotted line *a* represents the measurement of one inch below the left border of the base of the pulmonary artery, while the dotted line *b* represents the half-inch to the left side of this. The point of the knife is entered at the extremity of the latter, and is drawn downwards in the direction of line *c*, *c*.

fication of the coronary arteries following upon atheromatous endo-arteriitis. The muscular fibre becomes fatty, softens, and under some unusual strain gives way, the escape of blood in most cases causing almost immediate death.

Slit the coronary vessels open with a probe-pointed bistoury. If they are healthy they should have a bluish-pink tint and be quite smooth. Any other features of note on the surface should all be diligently recorded, such as an unusual size of either of the ventricles, etc.

simultaneously affected, remove the kidneys, ureters, bladder, and, it may be, urethra, without disconnecting them. The examination can be much better carried on out of the body than within it, and the parts can, moreover, thus be preserved entire as a permanent preparation. Slit the ureters open along their course, and notice whether the mucous membrane is congested or not, and whether there is any catarrhal discharge within them.

11. **The Bladder.**—It is advisable to remove the bladder along with the other pelvic organs. Cut through the peritoneum a little above the brim of the pelvis, and, introducing the hand behind it, tear asunder the loose cellular pelvic tissue. Cut across the urethra and corpus spongiosum a little beyond the prostatic part, and remove the vagina and rectum by an incision a short distance internal to the vestibulum and anus. Tear out everything in front of the curve of the sacrum, and cut off the peritoneum and attachments of muscles higher up.

If for any reason it is desirable to collect the urine, as, for instance, in a case where poisoning is suspected, draw it off with a catheter before commencing the inspection.

Open the bladder by an incision in front. Examine the mucous membrane with great care for congestion, abrasions, or a catarrhal condition, and observe the character of the urine that may be contained within it. Cut through *the prostate*, and notice its size and texture. Squeeze it, and see whether secretion of any kind comes out of the ducts. It is sometimes advisable to remove the testicles in connection with the entire urinary organs.

12. **Supra-renal Capsules.**—Be careful not to omit the examination of these in all cases; they are apt to be forgotten. Naked-eye examination, unfortunately, yields little definite information as to their condition, unless some very gross disease be present, and hence, as often as possible, the microscope should be called in to assist. It requires a good deal of experience to be able to say even with the microscope when they are morbid, or rather, when they are healthy.

13. **The Œsophagus** cannot be well examined until the larger thoracic viscera have been excised. Its diameter should be taken with the cones at different parts, and it is to be slit up with a pair of intestine scissors. It is well to retain it in connection with the stomach. Notice the state of the mucous membrane, and in cases of spasmodic stricture examine it very carefully for small follicular ulcers. They are sometimes the cause of extreme dysphagia.

14. **The Stomach and Intestines** should be removed in cases of death by poisoning before any other organ, care being taken to ligature the lower end of the œsophagus and upper part of the duodenum. Under such circumstances (indeed under any circumstances) the stomach should not be opened *in situ*. No object is gained thereby, unless where an ulcer has become adherent to the liver or other viscus; and, even here, there is no cogent reason why the stomach should not

first be removed. If it be adherent to other viscera, remove the whole *en masse* and examine the parts when they are spread out on a convenient surface. They should of course have been previously described as they lay in position.

Where a person is suspected to have died from poison, the method of removal of the stomach and duodenum, or it may be the whole intestine, is of primary importance, and the operator should attend to the following points:—(*a*) Pass a *double* piece of waxed strong twine round the upper part of the pharynx. Tie it in several knots, twist it again round the pharynx, and tie a second time. Leave a long end, so that there is no danger of the knot coming loose. (*b*) Ligature the lower end of the duodenum in the same way. (*c*) Remove the œsophagus, stomach, and duodenum, having previously ligatured the intestine. (*d*) Procure a perfectly clean wide-mouthed bottle which has not been previously used for any purpose. Cut the duodenal ligature, and place the end of the duodenum in the bottle. Raise the œsophagus gently and allow the whole contents to flow into the bottle. (*e*) Put the stomach and attached parts into a second bottle.

Cut the cardiac ligature and open the lesser curvature of the organ by an incision about 3 inches long. Introduce a cone, and measure the two orifices. Complete the incision in the lesser curvature by connecting it to the œsophagus on the one hand, and to the duodenum on the other, so that the organ is laid open from duodenum to œsophagus along the lesser curvature. Look over the mucous membrane, noting the amount of blood within it, the colour of congested parts, erosions, ulcers, or any other appearances which seem to be abnormal. If there is any unusual colour, describe this with care. A dark slate colour or a black precipitate is usually due to the patient having taken some metallic compound, medicinally or otherwise, which is decomposed by sulphuretted hydrogen. Grasp the pyloric ring and feel whether it is in any way indurated or otherwise altered.

After carefully noticing the condition of the omentum and mesentery while the intestine is still attached to the latter, *remove the intestine* with the sectio knife by seizing the most prominent loop (any loop), and cutting off the mesentery close up to its insertion. Do not leave portions of the mesentery adherent, as they throw the intestine into coils when it is being washed out, and prevent its being easily opened with the bowel scissors. Detach the small from the large intestine about 1 foot above the ileo-colic valve.

In typhoid fever it not infrequently happens that the lowest Peyer's patch is the enlarged and ulcerated one, and hence if the small intestine is cut off immediately above the valve this is apt to be destroyed. Wash out the contents of the intestine by attaching the bowel to a water tap, and notice the colour, consistence, etc., of the fæcal matter. Lay the bowel open with the bowel scissors while water is running through it, pulling the intestine against the scissors and not pushing the scissors into the intestine. Cut on the mesenteric side, as it is not desirable to wound the Peyer's patches which lie opposite.

Always begin the examination of the mucous membrane at the

upper end, noting the colour, amount of blood, enlargement of the solitary follicles or of Peyer's patches, etc. If there is any suspicion of waxy disease, treat the mucous membrane with iodine solution. There is no naked-eye sign by which the waxy intestine can be detected, and hence the necessity of applying iodine to it more frequently even than to other organs. The same rules hold good for the examination of the large intestine as for that of the small.

15. **The Mesenteric and Prevertebral Lymphatic Glands** should be examined along with the mesentery.

16. **The Pancreas** is so seldom diseased that its examination is frequently neglected. In a carefully-conducted examination this should not be so, and the best time to remove it is after the intestine. The duodenum should have been previously either detached or, if the pancreatic duct is to be inspected, it may still be kept in its natural position. The commonest disease of this viscus is cancer, situated in the head, and either primary or secondary to a primary cancer of the stomach.

17. **The Semilunar Ganglia** have been the subject of examination in diseases of obscure origin more of recent years than formerly. Seeing that they are so closely connected with the nervous supply of the abdominal viscera, it might be expected *a priori* that they would be frequently diseased. Their examination, however, so far as it has gone, has proved somewhat unsatisfactory. The cœliac axis is the guide to their position.

18. **Aorta and Vena Cava.**—It is unnecessary to detail at greater length the rules to be followed in examining other parts of the thoracic and abdominal cavities, further than to remind the operator to remove the whole aorta and iliac arteries after the other abdominal and thoracic viscera have been taken out. Where the person has died from asphyxia, examine the ascending vena cava before any of the other abdominal viscera have been touched, and before the heart has been removed. It looks like a large blue coloured sausage in such cases from the large quantity of blood within it.

19. **In typhoid fever** *cut into the adductor muscles of the thigh and the flat muscles of the abdominal wall.* They assume a peculiar pallor due to a colloid change in the sarcous substance (Zenker No. 2). The muscular tissue of the diaphragm should likewise be examined in this disease, as it also suffers, although in a minor degree, from the colloid degeneration.

20. **Mouth, Larynx, and Pharynx.**—Notice the condition of the gums and teeth, and whether there is any alteration of the tongue such as the protrusion in myxœdema, or lymphangeiomatous macroglossia. Remove the tongue, larynx, and trachea together in the following manner:—Extend the primary incision along the front of the body up to the chin. It need not pass into the face as this leaves an unsightly mark. Cut off the attachments of the muscles to the inner aspect of the lower jaw, dividing the mucous membrane at the same

time. Pass the forefinger into the mouth and draw the tongue downwards, and, while doing so, divide the pharyngeal muscles and separate all attachments back to the spine and as far down as the bifurcation of the trachea. The œsophagus, if not previously removed with the stomach, ought to be taken out in its entire length along with the other parts. Examine the larynx and pharynx for foreign bodies. See whether the true vocal cords close properly, or whether they are ulcerated, tubercular, œdematous, or covered with a croupous membrane. Slit open the larynx posteriorly, and continue the incision down through the trachea and primary bronchi. Notice the condition of the mucous membrane as regards congestion, false membranes, tubercles, etc.

In all medico-legal cases the larynx should be examined even where the cause of death seems to be apparent, and in cases of unexplained sudden death it would be an unpardonable oversight to omit doing so in any examination, whether of a forensic nature or not.

21. **Examination of the Head.**—A question from the medical jurist's point of view comes to be whether the brain ought to be examined before the heart or *vice versa*. Can any alteration be caused in the amount of blood in either organ by removing the one before the other? Medico-legal experts seem to differ in their opinion on this subject, and hence, in order to err on the safe side, it is expedient to expose both organs, and to examine them simultaneously in reference to the amount of blood within them. The cranial cavity being air-tight, and the exterior being sufficiently rigid to be uninfluenced by atmospheric pressure, it would only be after the calvaria is removed that the vessels could possibly lose any quantity of blood. The removal of the heart probably does not make much difference in the amount of distension of the blood-vessels of the brain and its sinuses, but in order to avoid any legal quibble which might arise upon the supposed possibility of such occurring, the recommendation to display both organs before cutting into them seems to be wise. The heart ought to be exposed first, as it might be argued that the removal of the rigid skull-cap previous to the examination of the heart allowed some of the cerebral blood to regurgitate.

The scalp has of course been examined for any sign of a wound, bruise, tumour, skin eruption, etc., before commencing the internal examination. An incision is next made from ear to ear through all the soft parts, the head being supported by a block placed under the neck. The two flaps thus mapped out are reflected so as to leave clear room for the working of the saw. The temporal muscles should be scraped from the bone or an incision be made through them at the point where the saw is to be applied, and this incision should be carried circularly round the whole pericranium so as to leave the bone free. An assistant now holds the head, his hands being protected by a strong towel, and the *outer* plate of the skull is sawn through. The incision should not go deeper, as otherwise the soft parts are sure to be injured. In medico-legal cases where some injury to the head is suspected, an exception is made to this rule. It is injudicious to use a mallet under such circumstances, and hence the whole depth of the skull-cap must be cut through.

In ordinary cases, however, the outer plate alone is to be divided, and the remaining deep plate chipped off with the chisel and mallet. The blunt hook described under the *armamentarium* (Sect. 1) is very useful in catching hold of the skull-cap and dragging it off where the employment of a mallet is inadvisable. If the dura mater is so adherent as to prevent it from being dragged from the bone, it should be cut all round, and left attached to the skull-cap. As a rule, however, there is not much difficulty in removing it. Cut it round with the probe-pointed bistoury, after examining the surface and noting the state of the skull-cap and meningeal vessels. Cut through the falx anteriorly, but do not remove it from the longitudinal sinus, because, if the brain has to be injected with a hardening fluid, this is apt to disturb the vessels. Examine the exposed surface of the brain. Cut the nerves with scissors, and remove as much of the internal carotid artery as possible. Run the probe-pointed bistoury through the tentorium cerebelli on each side so as to liberate the cerebellum. Cut the spinal cord across through the foramen magnum as low down and as nearly transversely as possible; divide the vertebral arteries; insert the forefinger into the foramen and withdraw the medulla. Lastly, divide the remainder of the dura mater at the torcular after the brain has been removed from the cranial cavity. Place the organ on some convenient support, such as a hollow dish, the skull-cap itself, or a folded towel, and before proceeding to its description inspect the base of the skull. If a fracture is suspected, remove the dura mater with the chisel. Be careful not to mistake a mere vascular impression on the bone for a fracture. Lay open the chief sinuses.

Returning to the brain itself, the pathologist must settle in his mind whether the organ is to be cut into at present, or whether it is first to be hardened.

In all important nervous cases where a typical lesion is suspected, certainly *harden it first*. As this takes from six weeks to two or three months to accomplish, it naturally requires considerable self-denial to resist the temptation of investigating the cause of the disease there and then. If the physician in charge of the case can be persuaded to forego this temptation, the result will be ample recompense.[1] The advantages of pursuing this course are the following:—(1) The organ is in such a firm tough condition that it can be handled with impunity. (2) When cut into, the exposed surface is beautifully defined on account of the grey and white being so sharply separated. (3) All the sections can be kept as permanent preparations. (4) It is equally useful for naked-eye or for microscopic work. (5) Any lesion causing softening is far more distinctly demarcated than in the fresh state on account of the softened tissue being fixed.

It is only by hardening the organ before incising it that we shall ever make any progress in the accurate localisation of lesions in important nervous cases. What could be more indefinite than the usual description of the localities in which lesions of the brain are situated? In the majority of cases, the reports are untrustworthy, a misfortune that can in great part be avoided by hardening the organ in the manner recommended. It must be borne in mind that as the Müller's fluid employed in hardening has to be injected from the two carotids and the one vertebral, these vessels must be got out with as little injury, and as long, as possible.

If it be a case of no particular clinical interest, cut into the organ at once; it is not necessary to harden it. Before doing so, however, remember *to weigh it*, and to examine the surface. Look carefully over the regions of the base, the Sylvian fossæ, the upper and lower surfaces of the cerebellum, and the fissure of Rolando for the

[1] For method of hardening see Chapter V.

presence of tubercles or for evidence of meningitis. Tear open the Sylvian fissure, and follow the course of the middle meningeal artery. Do not mistake the Pachioni's granulations at the vertex for tubercles.[1] Note the presence of every lesion relatively to the convolutions or to other named structures. Measure the superficies and depth of all lesions.

In former times the brain used to be opened by Virchow's method, that is to say, by a series of fore-and-aft sections exposing the ventricles and medullary substance without detaching any of the parts. Nothing could be better than this method for displaying a gross lesion in the basal ganglia or ventricle, such as a recent hæmorrhage. Still, it is fraught with many disadvantages when our object is to localise a small and, it may be, a somewhat indefinite lesion. Further, if the parts are to be afterwards employed for microscopic examination, the continuity of one segment with the other becomes uncertain. It is therefore preferable to open it by a series of perpendicular slices. This latter method is also superior to the former in the fact that as the relationship of the capsules and basal ganglia is retained, the segments, if thought fit, can be preserved as permanent preparations. The old system in the Edinburgh Infirmary used to be that of removing the organ in horizontal slices while it still lay in the skull, and, in many respects, it was excellent. The *beau ideal* of a method for exposing a lesion is an impossible one, namely, that of slicing the organ both perpendicularly and horizontally.

Where are the incisions to be made? Pitres (No. 3; and No. 4, iv. 1877, p. 245) gives the following directions for making perpendicular transverse sections calculated to expose the most important parts. He calls each incision by a special name, according to the locality in which it lies.

Beginning in front, the first runs through the prefrontal region, or that part of the organ anterior to the motor centres, and is known as the *prefrontal section*. The second cuts the bases of the first, second, and third frontal convolutions, and is located two centimètres anterior to the fissure of Rolando. It goes by the name of the *pedunculo-frontal section*. The third he names the *frontal*, dividing as it does the ascending frontal convolution, parallel or nearly so with the fissure of Rolando. The fourth, or *parietal section*, bisects the ascending parietal convolution. The fifth is the *pedunculo-parietal section*, situated three centimètres behind the fissure of Rolando. The sixth and most posterior of all is the *occipital*, cutting across the occipital lobe.

Although this system is a step in the right direction, yet, in making the sections, it will be found that they do not always expose the same parts. The reason of this is that what is seen entirely depends upon how the brain is lying at the time it is opened, for although the fissure of Rolando may be taken as a standard of direction, yet in making the sections behind this the brain is very apt

[1] This mistake was evidently made in a comparatively recent criminal case, and served to defeat the ends of justice.

to get misplaced, and the direction of the incision, and, consequently, the parts exposed, will naturally vary. As these sections, moreover, run parallel with the fissure of Rolando, it is manifest that they cannot be perpendicular. Besides this, the cerebral peduncles are cut perpendicularly or obliquely, whereas it will be admitted that a much better view of these is obtained when they are transversely incised.

The first procedure which ought to be adopted in order to avoid these objections is to remove the pons, cerebellum, and medulla by a cross incision through the middle of the crura cerebri cutting straight backwards into the substantia nigra and anterior corpora quadrigemina, and thus detaching the pons and medulla from the other portions of the brain. A progressive series of transverse incisions is now carried throughout the pons and medulla each about one-eighth of an inch

FIG. 5.—PERPENDICULAR TRANSVERSE SECTION OF HUMAN BRAIN—SECT. I.

thick. The segments should not be detached from the pia mater, if possible, but left connected and in sequence, so that they can be readily replaced. They may be employed for microscopic examination afterwards, for which purpose longitudinal or oblique sections are almost useless.

As just said, unless the brain is fixed in one constant position, perpendicular sections will always vary in what they show. Even in the most accurately made sections of two brains the exposed parts are never always quite alike, although the great landmarks may be the same in both. The method to adopt in order to fix the organ in some definite position is to lay it, vertex downwards, *with the tips of the occipital and frontal regions in one horizontal line.* The organ should be placed upon a board, as it is easier to cut on this than on any other

surface. The number of incisions, and where they ought to pass through, depend very much on what parts one wants to expose. For ordinary purposes, however, the brain may be sliced through the following seven localities. It will be found that the sections thus made expose the parts of greatest importance.[1]

Section I. (see Fig. 5) **runs through the anterior half of the third frontal convolution** and exposes the *tractus internus*, *medius*, and *externus* (seen on left side), and the *oval-shaped area* (seen on the right.[2])

Section II. (see Fig. 6) **runs through the tip of the temporo-sphenoidal lobe and operculum.** It shows the heads of the *caudate* and *lenticular nuclei* with the *inner capsule* separating them, the

FIG. 6.—PERPENDICULAR TRANSVERSE SECTION OF HUMAN BRAIN—SECT. II.

island of Reil and *unnamed white substance* belonging to it, the *corpus callosum* and *septum lucidum*, with the *fifth ventricle.* The figure also displays *one of the roots of origin of the olfactory*, and the *nipple-like process of gray matter* to which the olfactory tract becomes attached in the sulcus olfactorius. The *temporo-sphenoidal lobe* is still disjoined at this level from the rest of the brain.

Section III. (see Fig. 7) **is made immediately in front of the**

[1] The accompanying figures of the parts seen in these sections were drawn from preparations made by the author's gelatine-potash method. They were all traced upon gelatinised glass from the preparations themselves, and can be relied upon as faithful representations.

[2] For explanation of these terms, see author's paper on the "Corpus Callosum in the Adult," in the *Journal of Anatomy and Physiology* vol. xix.

optic chiasma. It cuts through the *temporo-sphenoidal lobe* shortly after it has joined with the rest of the brain. It exposes the head of the *caudate nucleus* and two divisions of the *lenticular nucleus*, the *corpus callosum*, *septum lucidum*, and *fifth ventricle*. The front part of the *anterior commissure* is also brought into view. The *three roots of the olfactory* are shown passing respectively upwards, inwards, and outwards.

Section IV. (see Fig. 8) **runs through the infundibulum.** It cuts obliquely across the *first frontal* and *ascending frontal convolutions*, and the *temporo-sphenoidal lobe*. It exposes the *middle part of the caudate nucleus*, the *anterior nucleus of the thalamus*, and adjacent *knee of the inner capsule* in which it lies imbedded. The *three divisions of the lenticular*

FIG. 7.—PERPENDICULAR TRANSVERSE SECTION OF HUMAN BRAIN—SECT. III.

nucleus are now brought into view with the two *striæ medullares* separating them, and even a fourth division of the ganglion is visible. Beneath the internal and middle divisions of the lenticular nucleus is the *substantia innominata of Reil*, composed of its three layers (Meynert), named respectively from above downwards, the *lenticular nucleus loop*, the *layer of gray matter giving rise to the posterior longitudinal bundle*, and the *lower peduncle of the thalamus*. Beneath the external segment of the lenticular nucleus is the *anterior commissure*, passing obliquely outwards into the temporo-sphenoidal lobe; while outside of the external segment of the lenticular nucleus are the *outer capsule*, *claustrum*, *white substance of the island*, and the *island of Reil* itself. Passing to the parts in the middle line, they are seen to be from above downwards, the *first frontal convolution*, the *gyrus, fornicatus*, *corpus callosum*, and *septum lucidum*,

FIG. 8.—PERPENDICULAR TRANSVERSE SECTION OF HUMAN BRAIN—SECT. IV.

FIG. 9.—PERPENDICULAR TRANSVERSE SECTION OF HUMAN BRAIN—SECT. V.

with the *remains of the fifth ventricle* within it. On either side of the septum lucidum is *the lateral ventricle*, with the *foramen of Monro* passing downwards to the *third ventricle*, which, it will be seen, is a mere narrow slit. Surrounding the third ventricle and forming its wall, is the so-called *gray substance of the ventricle* with the *fornix* imbedded in its substance. Coming still farther down, this gray substance merges into the *tuber cinereum* and *pituitary body*. At each side of the tuber is the *optic tract*, cut obliquely from its slanting position in running backwards, and outside of this again is the *anterior perforated space*. On the inner aspect of the temporo-sphenoidal lobe is a large tonsil-shaped mass of gray matter—the *nucleus amygdalaris*.

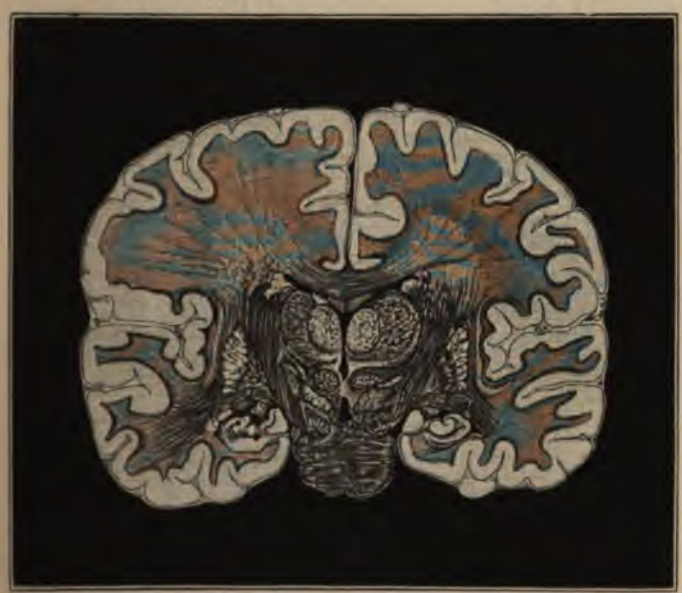

FIG. 10.—PERPENDICULAR TRANSVERSE SECTION OF HUMAN BRAIN—SECT. VI.

Section V. (see Fig. 9) **cuts through the corpus albicans**, and exposes the *thalamus*, *tail of the caudate nucleus*, and the *three divisions of the lenticular nucleus*. The *internal capsule*, its fibres descending to the pedunculus cerebri, is seen separating the *caudate nucleus* and *thalamus* on the one hand from the *lenticular nucleus* on the other. Within the thalamus lies the *band of Vicq d'Azyr*, and coursing along the inner concave aspect of the internal capsule is the *lamina medullaris externa*. Beneath the lenticular nucleus runs the *optic tract*, splitting into its two terminal divisions. Outside of the lenticular nucleus are the parts mentioned in the description of the preceding figure, namely, the *outer capsule*, *claustrum*, *white substance of the island*, and the *island of Reil*. Taking the place of the nucleus amygdalaris on the inner aspect of the temporo-sphenoidal lobe is the *cornu Ammonis* with the *descending*

horn of the lateral ventricle to its outer side. Notice that the gray matter of the cornu Ammonis is directly continuous with that of the lenticular nucleus. The *tænia semicircularis* is seen separating the caudate nucleus from the thalamus, and splitting into two branches which inclose the *anterior nucleus of the thalamus.*

Section VI. (see Fig. 10) **cuts through the anterior margin of the pons,**[1] and exposes the *pedunculus cerebri, substantia nigra, red nucleus, corpus Luysianum, thalamus, and tail of the caudate nucleus.* The convolutions incised are, beginning immediately above the corpus callosum, the *gyrus fornicatus,* the *paracentral lobule,* the *ascending frontal and ascending parietal,* the *first, second,* and *third temporal,* the *gyri occipito-temporalis lateralis* and *medialis,* and the *gyrus uncinatus.* The

FIG. 11.—PERPENDICULAR TRANSVERSE SECTION OF HUMAN BRAIN—SECT. VII.

lenticular nucleus is also seen, but is now rapidly becoming reduced in size, while the outer capsule is correspondingly increasing in dimensions. The triangular aperture immediately above the pons is not the aqueduct of Sylvius, but is simply the hollow or bay formed by the diverging pedunculi. The aqueduct has not as yet come into view. In the thalamus is seen a large oval-shaped gray mass abutting upon the third ventricle. It is the *median nucleus of the thalamus.*

Section VII. (see Fig. 11) **passes across the front of the angular gyrus.** Above is the *lobulus parietalis superior,* and below are the *occipito-temporal convolutions.* For convenience in description, it will be well to commence with the *posterior horn of the lateral ventricle,*

[1] In this and the following figure the pons is represented as left attached. In the method of cutting up the brain recommended, the pons and medulla would, of course, be removed.

which is exposed in the middle of each hemisphere. To its inner side is the *posterior extremity of the corpus callosum*, while below this is a little eminence evidently compounded of callosal fibres — the *hippocampus minor*. To the outside of the ventricle are seen two well-defined bands of fibres cut across. The internal of these, that which constitutes the outer wall of the ventricle, is the so-called *tapetum*, while the more external of the two is what is known as *Gratiolet's optic radiations*, or the parieto-occipital band. The lower part of the figure represents an oblique section through the *cerebellum*, *fourth ventricle*, and *medulla oblongata*.

22. **The Spinal Cord.**—With the sectio knife make an incision through the soft parts over the spine from the occipital protuberance down to the lower lumbar region. Dissect all the muscles and other soft parts back for such a distance that the spine is freely exposed, and, in doing so, lay the vertebræ quite bare. Several instruments are recommended for opening the spinal canal, such as a double saw to be applied simultaneously to the laminæ on both sides. A single small saw with a rounded belly has also been recommended, and a strong knife-like instrument with a hook at the end is sometimes included in pathological instrument cases, the hook being intended to slip under the laminæ while the sharp edge of the instrument is driven through them with a mallet. A pair of *very strong* bone pliers with long roughened handles is preferable to any of the above. One of the vertebral spines is first cut off, usually in the lower cervical region, the point of either of the blades is now insinuated under a lamina, and this is cut across. The corresponding lamina on the opposite side is similarly divided, and the piece of bone so separated is reflected back upon the spine, or seized with the bone-pliers and twisted off. The blades are next applied to the laminæ above this, there being plenty of space between the spinal cord and the bone to introduce them. If the instrument is sufficiently powerful, the laminæ are cut across with the greatest ease, and without any fear of injury to the cord. When the division of the laminæ is completed in a direction upwards, the process is continued downwards to the lower lumbar region, the pieces of bone as they are liberated being removed from the soft parts by twisting with the forceps. The time occupied in doing this, which otherwise is apt to be a very laborious operation, is so short, that five minutes should suffice for the complete removal of the organ from the time when the primary incision is made into the soft parts.

The cord having been thus brought into view must be removed with the dura mater. Its nerves should be divided by running a sharp knife down each side of the canal, and if it be desired to secure some of the ganglia, these should be detached along with the entire vertebra, and be subsequently dissected out. The branches of the cauda equina are next to be divided, and the dura mater covering the conus medullaris is to be seized with a pair of dissecting forceps. Care must be taken not to take hold of the cord itself, as it will be sure to suffer injury. As long

as the dura mater alone is drawn upon, there is no danger of injury, but pressure upon the cord is certain to bruise it, and to give rise to appearances which may afterwards be mistaken for something morbid. If the above directions be followed the cord should not have suffered the slightest injury. The connections of the ligaments of the dura mater are to be severed with a pair of scissors held in the right hand, while traction is exerted upon the membrane with the left. When removed, lay it out flatly upon an even surface with the posterior aspect downwards, and with a pair of scissors slit open the dura mater along the anterior aspect. Should it be desired to harden the organ, on no account cut into it, as the myeline is extremely apt to be driven out of the cut ends as the hardening is proceeding. Examine the cut upper extremity, but leave any further incising until the organ has become fixed with the Müller's fluid in which it ought to be placed (see Chap. V). If it is not to be hardened, cut it transversely into pieces of about an inch in length, leaving them still attached by the pia mater posteriorly. Notice the condition of the white columns and of the horns of gray matter. The naked-eye examination of the cord is always unsatisfactory, but when the columns are wasted or changed in colour as in locomotor ataxia, or when there are patches of sclerosis, these can be readily detected with the naked eye. Never trust to naked-eye examination alone, however, in any lesion of the central nervous organs. The condition of the *spinal canal* itself ought, lastly, to be inspected.

CHAPTER III

THE SECTIO CADAVERIS—(*Continued*)

General Instructions regarding the Naked-Eye Examination of Organs after they have been removed from the Body.

23. As method is the very essence of a good pathological report, it is essential not only to conduct the examination of the body previous to the removal of the viscera in a systematic manner, but to use similar precautions in describing the organs after they have been excised. The following order of examination, if attended to, will be found of great aid in attaining the necessary accuracy.

A. Weight.	F. The cut surface.
B. Size.	G. Colour.
C. Consistence.	H. Squeezing and scraping.
D. Surface and edges.	I. Odour.
E. General contour.	K. Microscopic examination.

A. **Weight.**—All organs, the heart excepted, ought to be weighed before they are cut into. This viscus frequently contains a mass of blood-clot, which, if weighed along with it, would render the result fallacious. On the other hand, if the other organs are weighed after being incised, the escape of liquids, such as the contents of cysts, abscesses, etc., also vilifies the result. It should be remembered that the weight is not always proportional to the size. Thus a fatty liver may be extremely large but at the same time specifically lighter than a normal organ or than one which contains a heavy foreign substance such as fibrous tissue or amyloid. From our unfamiliarity with what a hundred or a thousand grammes of a particular substance represent in bulk in articles of daily use, one cannot form nearly so graphic an idea of what is meant, when these weights are applied to diseased organs, as when their weight is described in pounds and ounces. Hence it is perhaps preferable to employ the avoirdupois pound, until the decimal system becomes more general in this country.

Average Weight of Normal Organs.

Liver, 3 lbs.	Left Lung, 1 lb. 4 oz.
Kidney, 5½ to 6 oz.	Right, 1 lb. 7 oz.
Spleen, 5 to 6 oz.	Heart, 10 to 13 oz.

Brain, 49 to 50 oz.

The organs in the female are usually less in weight than those in the male.

B. **Size.**—Where a new substance is infiltrated into an organ, the latter is generally enlarged, as in the *wax-like* and *fatty* infiltrations. It may happen, however, that two new substances are present in an organ or tissue, the one tending to enlarge its bulk the other to diminish it, and it depends upon the preponderance of the one or the other as to what the result will be. A liver is often simultaneously the subject of cirrhosis and of the *amyloid* or *wax-like* disease, and, in such circumstances, usually is a small organ, the reason of course being that the destruction of liver tissue by the pressure of the cirrhotic bands is greater than the wax-like substance will compensate for. Two organs, again, may be affected with the same disease, the one being small the other large. The most familiar example of this is the cirrhotic liver, where in one variety the organ may be wasted to a third of its bulk, and in another may be twice its original size. The explanation is that the cirrhotic fibrous tissue is so abundant in the large that it more than makes up for the loss in the liver substance.

Remember that a *large* is not necessarily an *hypertrophied* organ. Many of the largest diseased organs are in the last stages of *atrophy*. It is an unpardonable mistake to suppose that *hypertrophy* and *enlargement* are synonymous terms, or that atrophic organs are always small. Diminution in size is a common attribute of an atrophic organ, but is not invariably associated with it. Thus the waxy and large cirrhotic livers are both usually much over the normal bulk, but no one with the most elementary knowledge of pathology would think of calling them hypertrophied organs. The terms *growth*, *hypertrophy*, and *atrophy* must all be specifically defined, otherwise we get into endless confusion. (See Chaps. X. and XI.)

It would be extremely desirable if we could invariably adopt the decimal system of linear measurement in this country for all medical purposes. Unfortunately the same objection holds good for this as for measurement by weight, namely, that the majority of people in this country are not sufficiently familiar with the length of a mètre or a centimètre to make these standards of everyday use. Hence it is preferable to express the gross measurements of organs in inches, or to employ the metric system along with this.

It is a good rule to avoid the terms *large* and *small* as much as possible. They are relative terms, and are liable to great abuse in pathology, the employment of them being entirely based upon the subjective notions of the pathologist. The majority even of advanced students have the mistiest conception of the size of the normal organs, and hence, in order to avoid any mistake, the use of these terms should be discouraged in all descriptions. There are some pathological objects,

however, which are so irregular in shape that they cannot be measured with convenience, and, in such cases, an approximate notion of their size can be obtained by likening them to some familiar objects. Thus seeds and fruits in common use, and of a specific shape, are convenient, but care should be taken in instructing beginners that they are familiar with the bodies employed in comparison. Nothing is commoner than to find students liken bodies in size to a millet seed, yet it will be found that with a few exceptions the average student has never seen millet. It is well, therefore, in order to ensure accuracy of comparison, to have, as in Virchow's laboratory, a number of standard bodies at hand so that they can be placed side by side with the body under comparison. If extreme accuracy be desired in estimating the bulk of a morbid object, its displacement measurement should be taken. In the case of the brain this is by far the best method to follow, but with other organs it is not usually necessary to do so.

C. **Consistence.**—There is, unfortunately, no means unless that of practice and experience by which the normal consistence can be estimated. The natural consistence of the kidney may be likened to this, that, and the other thing, but there is no description which will ever teach a man what it actually is until he has passed many kidneys through his hands.

Do not test the consistence of an organ by pressing it with the tips of the fingers against a hard surface. The softest organ feels tough and resistant under such a method of examination. The only means by which any information can be obtained of its consistence is by taking the whole organ up in the hands. If it is flabby the edges will hang down on all sides; if it is rigid it does not tend to collapse; and if it is doughy in consistence it leaves the impress of the fingers upon it. An organ may be tough and at the same time elastic, as in the case of the amyloid liver; where, on the other hand, there is excess of fibrous tissue within it, the consistence is tough but inelastic, like the feeling of a piece of wet leather. A liver infiltrated with fat pits readily on pressure, and may be said to have a "doughy" consistence.

D. **Surface and Edges.**—In describing these, take notice of any roughness or unusual smoothness, the presence of tumours, adhesions, etc. Notice any irregularities of the edges, and whether they are infiltrated or attenuated. When a new substance is present in large quantity in an organ, the edges are usually more or less blunted and infiltrated as in the fatty and wax-like liver; but if the organ has suffered acute wasting, its edge will almost certainly be thin and sharply pointed, as in acute yellow atrophy of the liver, in which disease the organ sometimes has a parchment-like feeling from the loss of parenchyma.

E. **General Contour.**—In syphilitic diseases of the various organs, typically in the syphilitic liver, the contour is grossly altered. A liver in such a case may be difficult to recognise as such, from the deformity that has been brought about in it by the contraction of cicatrices. Where this alteration in general contour exists, it ought of course to be the subject of special description.

F. **The Cut Surface.**—Up to this point the organ is not supposed to have been cut into. It must now be opened by a single cut, or by a series of incisions made in particular directions. How are we to commence the description when the interior is exposed? The best rule is to describe first that which seems to be most abnormal or of most importance. Thus, for example, if a tumour be situated in the centre of the liver, commence with the tumour, and describe its surroundings subsequently. If the colour be the most striking feature, begin the description, with this, and so on. Above all things, finish the description of the exterior before proceeding to the interior. Take notice of the smoothness, lustre, moistness, dryness, or greasiness of the exposed surface, and of the quantity of blood which escapes when the incisions are made. The size of the cut vessels, and any degeneration of their walls, should all be diligently recorded.

G. **Colour.**—Of all the points enumerated in this list, colour is the most difficult for a beginner to describe. The majority of people never think of colours, and when they come to describe them, consequently make some remarkable mistakes. One of the commonest is to describe a pale organ as "white"—"The large white kidney"! So-called white objects in morbid anatomy are usually yellow or pale pink in tint, the former colour being frequently an important indication of fatty degeneration. Another common error is to describe an organ as of a "pale colour." *Pale* is not a colour, it is a degree of colour.

As the artist's standard of the various colours is a purely arbitrary one, and as it is an impossibility to tell exactly when yellow passes over into orange or blue into green, it is necessary in describing colours with accuracy to get to know those shades that are considered typical; and there is no better field for educating the sense of colour than that of morbid anatomy, the hues being so varied and subtle and the one coalescing so insidiously with the other. It is necessary in describing a part as having a certain colour to specify the particular variety. There are all degrees, for instance, of the colour "yellow," so common in morbid organs, each having a certain pathological significance. Cream yellow is generally the tint of an organ that contains fat; canary yellow is that resulting from bile staining; ochre yellow is the colour of the acute yellow atrophy of the liver; and an old hæmorrhagic cavity in the brain is stained orange yellow. The commonest blue colour is that which is found as a result of *post-mortem* decomposition, and may be described as a "slate" blue. Different shades of red are, of course, very common, and some of the transitional stages, where they become tempered with brown, are occasionally very difficult to describe. A little attention to the matter of colours will soon make the student proficient in their detection, provided, of course, he is not actually colour-blind.

The colours which follow upon *post-mortem* decomposition are varied in hue, and are most commonly met with in the abdominal cavity or on the surface of the body. Their cause is the *chemical decomposition* of the iron of the blood by the sulphuretted hydrogen set free in the gastro-intestinal canal, or from putrefying tissues. Remember that *post-mortem* staining of a livid or almost black colour does not always signify that the part is in a state of putrefaction (see Gangrene). It

simply means that chemical decomposition has occurred by sulphuretted hydrogen being liberated from some source and coming in contact with blood. Sulphuretted hydrogen seems to pass very readily through the coats of the stomach and intestine after death, and hence adjacent viscera have frequently a livid or black colour.

The colour of the surface of the organ is to be noted first; that of the cut surface should then be described. In the case of the liver, the centre of the lobule is often of a deep red, the periphery of a cream yellow, or there may be some other difference in hue of the centre and periphery. It is sometimes difficult to say which is at the periphery and which at the centre, and great care should consequently be taken to determine this. If a colour is suspected to be due to decomposition make a shallow cut into the coloured part. If this surmise is correct the colour will seldom be found to penetrate deeper than an eighth of an inch.

H. **Squeezing and Scraping.**—When an organ or tissue is œdematous it should pit on pressure, and when squeezed, the liquid it contains should be capable of being thoroughly expressed, so as to leave the tissue in a collapsed state. The lung is of all organs the most liable to œdema, and it may be sometimes difficult to tell by unaided vision whether the infiltration is pneumonic or not, whether it is liquid or solid. Squeezing at once settles the question, for if the air vesicles can be thoroughly emptied of their contents, and if the expressed liquid be serous in character, then the infiltration is not pneumonic. In acute catarrhal pneumonia, and in the softening or purulent stage of croupous pneumonia, squeezing may also serve to empty the infiltrated part. The expressed liquids are not, however, serous, but respectively muco-purulent and purulent. Be judicious, however, in squeezing a part. Nothing is more heart-rending to a histologist than to see the ruthless manner in which a delicate tissue is sometimes subjected to the Herculean grasp of some unsophisticated person. In testing an infant's lung, where there is a question of the infant having breathed, a piece of the organ should be compressed within a towel, and if the child has inspired the piece will float in water even after this.

Scraping the surface with a scalpel is of use when an organ is fatty or when it is desired to remove some of the cells of an organ or tissue for microscopic examination. The greasy débris left on the blade of the knife from the fatty liver is very characteristic. Other occasions will naturally suggest themselves, on which this method of examination may be of use.

I. **The odour** of the viscera is sometimes of importance. Thus, in diabetics, the acetone-like odour is a good diagnostic sign, especially if the organs have been kept in a closed box or bottle for twenty-four hours. It seems to increase by exposure to the action of the air. In leucocythemia the odour has the peculiar mawkish character of freshly-drawn pus. In persons who die during an alcoholic debauch the abdominal

viscera have a powerful butyric-acid-like odour. The smell of the contents of the stomach of course should be carefully investigated in criminal cases.

K. **Microscopic Examination of Tissues in the Fresh State.**—All morbid tissues should be examined microscopically while untouched by any hardening reagent and a note kept of their appearance to be compared with that of the tissue when it has been specially prepared. We thus make sure that any abnormalities are not caused by the medium employed for hardening, and also get an immediate, although it may be unsatisfactory, idea of what the minute alterations of the tissue are. Some parts are never the same after as they were before being hardened, and pre-eminently does this hold good of the brain cortex. By no subsequent means can this be studied so well as in the fresh state, especially when Sankey and Lewis' method of staining is employed. Most tissues are, as a rule, however, improved by the action of the hardening reagent, as it destroys their hygroscopic properties, and renders their outline more distinct than before.

Tissues about to be the subject of microscopic examination in the fresh state should not have touched water. They may be cut in various ways, the chief of which are the following:—

1. By means of a Valentin's double-bladed knife.

2. By embedding the tissue between two pieces of hardened amyloid liver, and cutting the section with a razor or flat brain knife. The piece of liver with contained tissue is held in the left hand, and the knife, previously moistened with a $\frac{3}{4}$ per cent common salt solution is made to pass through both with a single sweep.

3. A section may be cut simply from the organ itself with a sharp razor or flat knife.

4. By far the best method is to employ an ether freezing microtome, such as one of those recommended in Section 39. Moisten the surface of the cylinder with a little gum, and lay a slice of the tissue not more than $\frac{1}{3}$th of an inch thick upon it. *Freeze the tissue half through* and take one or two sections from the part where the frozen and unfrozen parts meet. The majority of tissues are ruined if frozen through completely, but if frozen half through there is always a level from which a few sections may be obtained which are uninjured. These alone should be used for microscopic work.

Place the sections in a small white basin containing $\frac{3}{4}$ per cent salt solution, and float them on to a slide. They are often filled with air-bells at first, but if left for a night, or sometimes even for an hour or two, they will disappear. If the section shows any marks of the ice crystals it should be rejected. Place a cover glass over it and examine it microscopically, first with a low power (50 diam.) and subsequently with a high. It may be stained, but this, with certain exceptions, is never so successful a procedure as when the tissue has been hardened. The examination of the fresh section in the above neutral salt solution without staining is usually far more instructive than when it is stained

and mounted in some permanent medium. Perosmic acid ($\frac{1}{2}$ to $\frac{1}{8}$ per cent solution in water) may be employed to advantage with *fatty tissues*, and the various tests for the wax-like substance can be similarly applied. Dilute acetic acid is particularly useful in demonstrating nuclei and in clarifying albuminous precipitates, and glacial acetic acid or a strong solution of potash for showing micrococcus or other micro-organisms.

If the tissue is of interest, several pieces ought to be hardened by the methods recommended in Chapter V.

Note-taking and Medico-Legal Reports.

24. In the remarks introductory to what has been said of the making of *post-mortem* examinations, the general principles on which notes ought to be taken were indicated. It now remains to discuss the subject a little more in detail.

In order that notes may not end in being cumbersome and irrelevant, it is sufficient to *describe only what is morbid*, merely mentioning generally that other parts having a special bearing upon the case were normal. In a case of sudden death, for instance, where the cause is not evident, it would be well to note that the heart fibre was examined but appeared to be perfectly healthy, or that the respiratory passages were clear and in a normal condition, but, as a rule, where the cause of death is apparent, as little superfluous matter as possible should find its way into the report. In medico-legal cases this is specially to be remembered. What the crown authorities want is a clear statement as to the cause of death, and although it may have been necessary to go into much detail in conducting the inspection, yet it is not necessary to describe the whole of this in the report if it is found to be unconnected with the actual cause of death. A general statement should be appended to the end of all medico-legal reports to the effect that "other organs were normal," or "were normal with the exception of" so and so, mentioning particulars as briefly as possible if they have no special bearing upon the case. The introduction of extraneous matter in a criminal report simply causes confusion in the minds of the jury, and is apt to lead to difficulties in a cross-examination that the witness may not have anticipated.

The form of outline notes that the author is in the habit of employing in the *post-mortem* room may be considered to be brief by many. It will be found, however, to be quite sufficient for all practical purposes, and to leave room for some individuality of description. It is best to have it printed, but if such facilities are not at hand, it ought to be written out *before the examination commences.* The collected reports can be subsequently bound up in book-form.

OUTLINE-FORM FOR TAKING NOTES AT *Post-Mortem* EXAMINATIONS.[1]

No. of Case. Page

NATURE OF THE CASE .....

.....

I. Preliminary Data.

Name ..... Age.....

Occupation.....

Ward in which patient died.....

Home address .....

Date of death..... 18.....

Date of examination..... 18.....

Medical attendant.....

II. History of Case.

III. External Appearances.

Height ..... *Circumference at shoulders* .....

P.-M. Lividity .....

.....

.....

Rigor mortis .....

.....

General nourishment .....

.....

Pupils .....

IV. Circulatory Organs.

(a) HEART.—*Weight (after being opened)* .....

..... *Pericardial sac* .....

.....

.....

Cone-diam. and competency of valves.			Size of cavities and thickness of walls.
Aorta	Compt.	Incompt.[2]	*Left ventricle* .....
Mitral	,,	,,	*Wall* .....
Pulm. artery ...	,,	,,	*Right ventricle* .....
Tricuspid	,,	,,	*Wall* .....

(b) AORTA (*thoracic*) .....

.....

.....

(*abdominal*) .....

.....

(c) OTHER ARTERIES OR VEINS .....

.....

.....

[1] The spaces here given are merely relative in size. They ought in actual practice to be considerably larger.

[2] Mark out one or the other term according to circumstances.

No. of Case.

V. **Respiratory Organs.**

(a) NARES .....

.....

(b) LARYNX AND TRACHEA .....

.....

.....

(c) LUNGS.

Left—Weight.....*Pleural cavity*.....

.....

.....

.....

Right—Weight.....*Pleural cavity*.....

.....

.....

.....

VI. **Cavity of Abdomen**—*Contents.*

Peritoneum .....

.....

.....

.....

VII. **Gastro-Intestinal Tract.**

(a) TONGUE.....

.....

(b) PHARYNX.....

(c) ŒSOPHAGUS .....

.....

(d) STOMACH—*Diameter of Pylorus*.....

Diameter of cardiac orifice .....

.....

.....

(e) SMALL INTESTINE .....

.....

.....

.....

(f) LARGE INTESTINE.....

.....

.....

.....

(g) RECTUM.....

.....

VIII. **Liver.**

Weight ..... *Gall bladder and ducts*.....

.....

.....

.....

.....

.....

No. of Case.

IX. **Pancreas.**

Weight .....

.....

.....

.....

X. **Genito-Urinary Organs.**

(a) KIDNEYS.

Left—Weight .....

.....

.....

.....

.....

.....

Right—Weight .....

.....

.....

.....

.....

.....

(b) PELVIS AND URETERS.

(c) BLADDER AND URETHRA.

(d) UTERUS, VAGINA, OVARIES, AND LIGAMENTS.

XI. **Supra-Renal Bodies.**

Left—Weight .....

.....

Right—Weight .....

.....

XII. **Spleen.**

XIII. **Nervous System.**

(a) HEAD.

(a) *Scalp* .....

.....

.....

(b) *Skull* .....

.....

.....

(c) *Membranes of Brain* .....

.....

.....

(d) *Brain—Weight* .....

.....

.....

.....

.....

.....

No. of Case.

(β) SPINAL CANAL.

(a) *Spine* .....

.....

.....

(b) *Spinal Cord and Nerves* .....

.....

.....

.....

XIV. **Other Organs.**

XV. **Addenda.**

XVI. **Microscopic Examination.**

XVII. **Opinion as to Cause of Death.**

FORM OF MEDICO-LEGAL REPORT.[1]

25. The foregoing form can be used for note-taking at any *post-mortem* examination, medico-legal or not, but the report that is sent in to the Crown authorities should not be in this shape. A report, as required in such cases, on the body of a person who died from fracture of the skull, is subjoined, which may serve to illustrate the manner in which it should be drawn up.

Medico-Legal Report in a case of Fracture of the Skull.

We hereby certify, on soul and conscience, that we this day (September 20th, 1880) examined the body of a man within the Royal Infirmary, Edinburgh, which was identified in our presence as that of

JAMES FARREL,
Residing at 4 Carrubber's Close, Edinburgh, by
Alexander Farrel, brother of deceased, and Susan Farrel or Kemp, the deceased's wife.

External Appearances.—The body was that of a strongly-built muscular man, 61½ inches in height, and 39 inches in circumference at the shoulders. It was well-nourished, the face pock-marked, and *post-mortem* rigidity was considerable in all the extremities. The dependent parts of the body, as it lay on its back, showed great *post-mortem* lividity, and the lips, scalp, ears, and tips of the fingers, also presented an extremely livid appearance. A stellate wound of the scalp, measuring superficially one and a half inch by half an inch, was found over the posterior part

[1] In England a Report is not usually required. The medical evidence is taken directly in the witness-box.

of the right parietal region. It passed down to the bone so as to expose this. The hair surrounding the wound was saturated with partially dried blood, and several spots of dried blood were also noticed upon the face and neck.

The Head.—The loose tissues between the scalp and the skull were found to contain a little recently extravasated blood for a distance of about half an inch to an inch around the wound. There was no sign of a bruise at any other part of the scalp.

An enormous recent clot of blood was found covering the whole left hemisphere of the brain situated between the Arachnoid and Dura Mater (two of the membranes covering the brain). It measured one quarter of an inch in thickness about the middle of the hemisphere. The brain at this part, and in fact over the whole hemisphere, was much compressed by the effused blood. The opposite side of the brain, although it was free from extravasated blood, was very dry and flattened. The tip of the left temporo-sphenoidal lobe (the middle lobe of the organ) was severely lacerated to a depth of about one-eighth to one-quarter inch. A large clot of blood lay firmly in contact with it. The interior of the brain did not present any abnormality.

The Skull had sustained a linear fracture of the right half of its occipital bone which extended upwards into the lower posterior angle of the right parietal bone. The length of the fracture was four and a half inches. A little recently extravasated blood was found within the fissure.

The Stomach smelt strongly of alcohol, and contained about three ounces of half-digested food.

Other organs normal.

Opinion as to Cause of Death.—From the above examination we are of opinion that the deceased James Farrel died from hæmorrhage over the brain, the result of a fracture of the skull.

Signed ....., M.D.
(Do.) ....., M.D.

Edinburgh, September 20, 1880.

Affixing of Labels.—Where it is necessary in forensic cases to retain the contents of the stomach, bladder, etc., or portions of organs for analysis or further examination, they should be placed in clean, unused bottles or jars. The bottles should be sealed, and a label affixed, descriptive of the contents, signed by the two subscribers to the report.

Literature Treating Generally of Post-mortem Examinations.—**Babes** (P. M. Exams. with a view to Bacteriological Research): Arch. Roum. de Méd. et Chir., i. 1887, p. 157. **Bourneville and Bricon**: Manuel de Technique des Autopsies, 1885. **Harris**: Post-mortem Handbook, 1887. **Orth**: Compend of Diagnosis in Path. Anat. (Eng. transl. by Shattuck and Sabine). **Virchow**: Post-mortem Examinations (Eng. transl. by Smith). **Woodhead**: Practical Pathology, 1885, p. 1.

CHAPTER IV

PREPARATION OF NAKED-EYE SPECIMENS FOR MUSEUM PURPOSES

26. MOIST museum preparations are of two kinds:—(1) Those which are to be used as hand specimens for demonstration; and (2) those which are to be permanently mounted in jars.

27. **Hand Preparations.**—All soft pathological preparations suffer by keeping. Their colour fades, and hence one most important element in their recognition is wanting. The cause of the colour fading is chiefly the extreme solubility of their hæmoglobin. If spirit is employed as a preservative, they become so rigid and so altered in colour and texture, as, in most cases, to be next to useless for teaching purposes or for future demonstration. Several other preservative solutions have been recommended, such as carbolic acid and glycerine, corrosive sublimate and glycerine, etc.

A mixture which will be found fairly serviceable for the purpose has the following composition:[1]—Make a saturated solution of arsenious acid in water by boiling. Filter, and, when still warm, mix together equal parts of this, of glycerine, and of methylated spirit. It is well to mix the glycerine and arsenious acid solution, to heat them, and afterwards to add the spirit. The advantages of this liquid are that it keeps the colour of organs better than spirit; it does not destroy their pliability; and it is a good preservative. If several organs are placed in one jar they should be separated by pieces of washed linen cloth, and a piece of the same, soaked in saturated solution of corrosive sublimate, should be placed over them. They should *not* be steeped for long in water before being placed in the preservative; it is usually sufficient simply to wash them. Hearts, livers, kidneys, lungs, and muscular structures keep beautifully in it. When used for demonstration, the organs ought first to be washed. It should be remembered

[1] Dr. Bruce of Edinburgh has lately employed a solution of biniodide of mercury (1 to 500 or 1 to 1000) with considerable success so far as keeping the colour is concerned. The fluid should be often changed at first.

that this liquid is suitable only for hand preparations—not for those mounted in glass jars.

28. **Jar Preparations.**—Organs which are to be mounted permanently in glass jars or other vessels in a transparent medium, must have been previously soaked in a running stream of water until the soluble colouring matter within them has been entirely washed out. As soon after this as possible, they have to be suspended in separate jars in the particular liquid in which they are to be retained.

If *spirit* is to be employed, they should first be hung in a mixture of 1 part methylated spirit to 2 parts water. This must be changed until the preparation ceases to throw down any precipitate. When the liquid remains clean the preparation is to be hung in the permanent jar in a mixture of equal parts methylated spirit and water. Care should be taken from the very first that the preparation hangs in the position it is ultimately intended to assume, otherwise it will become irremediably deformed. It is well to fill the jar in which it is to be placed first with water, so as to see that it hangs properly. If it does not sink in the dilute spirit load it with shot, which may, as in the most troublesome organ, the lung, be easily concealed inside. Do not load it with anything composed of iron, as this rusts and makes a mark. If at any future time a precipitate be thrown down, it can usually be got rid of by filtering through paper. The sort of tissue that is best preserved by spirit is one composed of a solid mass such as the liver or spleen. Delicate thin tissues such as intestine should not be placed in it, as it causes them to shrink. If a clean slice of an organ is desired, let it hang for some time in the dilute spirit, and after it has become fixed in shape cut into it.

For mounting all delicate membranous tissues and organs such as stomach and intestine, bladder, hydatids, uterine moles, and myxomatous tumours employ *saturated solution of boracic acid.* The solution is made by boiling an excess and allowing the superfluous acid to crystallise out in the cold. It is subsequently filtered through paper. If a membranous tissue is about to be preserved it should be stretched on a slip of glass of suitable dimensions, the stretching being effected by stitching the edges round the back of the glass. The thinnest of thread should be used. Tubercular, typhoid, and other diseased intestines should be placed in long jars. The intestine should cover one side only of the glass slip and be firmly stitched to it, so that it does not dangle about in the liquid.

Glycerine Jelly for Mounting Museum Preparations.—This is one of the most suitable media for mounting certain delicate organs such as the eyeball, brain, etc. It has the great advantage of solidifying round the organ and thus permanently fixing it in any required position. The glycerine jelly to be used for the purpose is differently composed from that employed for microscopic work. It is made in the following manner:—

Take of French gelatine 8 grm., glycerine 80 c.c., saturated solution

of boracic acid, made as just described, 240 c.c. glacial acetic acid, 20 m.

Soak the gelatine in the boracic acid solution, add the glycerine and the white of one egg, and shake the mixture thoroughly. Boil in a water bath, and when the white of egg has nearly all been precipitated, mix the glacial acetic acid. Continue to boil until the precipitate separates from the clear liquid. Filter through paper. If properly made, the jelly, when cool, ought to be perfectly transparent and almost colourless even when in a large mass.

Carbolic acid is frequently recommended as a constituent of glycerine jelly when employed for the present purpose. It is disadvantageous from being volatile, and from its bleaching any preparation stained with carmine. Boracic acid is sufficiently antiseptic to prevent the gelatine or the preparation from going wrong.

After soaking out all the blood in water, place the tissue preliminary to mounting, in a mixture of 1 part glycerine and 2 parts saturated boracic acid solution. It should lie in this for a fortnight or so until the solution has thoroughly penetrated, and until the preparation ceases to soil the liquid. Change the liquid as often as it becomes discoloured.

ORGANS SUITABLE FOR MOUNTING IN GLYCERINE JELLY.

29. A. **Ophthalmic Specimens.**—Dr. Priestly Smith gives the following directions (No. 6, 1880, i. p. 52). The media required are—(*a*) Müller's fluid; (*b*) Chloral hydrate, 1 in 20; (*c*) Glycerine and water, 1 in 4; (*d*) Glycerine and water, 1 in 2; (*e*) Glycerine jelly, made by soaking 1 part best French gelatine (Coignet & Co., Paris, "gold label,") in 6 parts water until swollen; heat and mix with it 6 parts glycerine; add a few drops saturated solution of carbolic acid, and filter hot through white blotting paper; (*f*) A thick cement made with oxide of zinc and copal varnish.

Immediately after excision the eyeball is placed unopened in Müller's fluid for three weeks, light being excluded. It is frozen solid and cut. It is next immersed in the chloral solution for some weeks, until all colour has been removed, still excluding the light. It is next put for twenty-four hours or longer in the weak glycerine solution (*c*), and is subsequently transferred for a similar period to the strong, after which it may be mounted in the glycerine jelly without shrinking. It ought to be held in position until fixed. When the jelly is cold and firmly coagulated, it is to be coated over with the white cement, and this again when dry with glycerine jelly to prevent cracking.

The receipt for glycerine jelly previously given (Sect. 28) will answer equally well, and is much more transparent.

30. B. **Brain.**—Where brain has to be retained in a thick slice, glycerine jelly is much the best medium to mount it in. It is first

hardened in Müller's fluid in the manner described in Chapter V. The Müller's fluid is next soaked out of it by steeping in solution of sugar of greater specific gravity than the Müller's fluid, and changing frequently, until all discoloration disappears. The segment to be preserved should be an entire section. The slice of brain freed from its Müller's fluid is now placed for at least a week, but longer if possible, in freezing fluid "B" (Sect. 37). When ready it is frozen in the large microtome (Sect. 39), and the surface is polished by shaving it like a piece of wood. The particular level which shows the lesion best can thus be exposed with the utmost nicety. The preparation ought now to be stained by placing it in the carmine staining fluid "e" (Sect. 43). The staining must be done very carefully the preparation being examined day by day until the requisite tint is attained, and should not be too deep. It should be thoroughly covered by the liquid, otherwise the staining will be partial. As a rule, three to four days is sufficient time. From the staining liquid it is momentarily transferred to water on a piece of glass, and is subsequently placed in the boracic acid and glycerine mixture previously mentioned (Sect. 28). Here it must lie for three to four days or longer, and if any carmine exudes into the liquid the latter should be renewed.

It is now ready for mounting. On the surface of a piece of ordinary thick window glass fasten four strips of plate glass 1 inch in breadth, with zinc cement (Sect. 46), in the form of a square or other quadrilateral figure, their broad surfaces being downwards. Run a little cement into the fissures between the pieces of glass, and allow it to dry. The size of the cell may vary according to the dimensions of the preparation, and too wide a margin should not be left, as this causes a needless waste of glycerine jelly. As a rule, a border 1 inch wide is sufficient. If a single thickness of plate glass is not sufficient to free the upper surface of the preparation from the cover, cement a second strip on the top of the first. Take care that the cement runs into all the fissures, and, in order to be doubly certain, it is well to put on an additional coating of zinc cement when the first is dry.

Pour into the cell sufficient glycerine jelly, made according to the receipt in Section 28, to half fill it, and draw out any air bells with a camel's hair pencil. Remove the section of brain on a piece of glass from the boracic acid and glycerine in which it is at present lying. Allow it to drip for a few minutes, and afterwards slip it gradually into the contents of the cell, in a slanting manner, so as to exclude all air. Fix it in the exact position required, and fill the cell with glycerine jelly as nearly to the top as possible. It is of advantage to place the cell upon a levelling tripod in order to fill it equally. Let the section remain for a night in this condition so as to solidify, taking care to exclude dust.

Next morning, with a camel's hair brush, coat the surface of the glycerine jelly with the boracic acid and glycerine mixture, and allow the superfluous liquor to run off. Prepare a cover made of a

sheet of common thick window glass, so large that it extends half-way over the wall of the cell. With a large pipette allow some melted glycerine jelly to run over the surface of that which has solidified. Slip on the cover glass, and leave the preparation to cool. When the jelly has thoroughly set, clean all off up to the edge of the cover, and cement the edges with asphalt as follows:—Roll out some thick slabs of clay and cut several strips about 1 inch broad, longer than either of the four sides of the cell. Join these round the cell at a distance of about half an inch from its edge, and into the space so enclosed pour the asphalt recommended in Section 32, at as low a temperature as is consistent with its melting. The asphalt should be allowed to include the edge of the cover-glass for a distance of about a quarter of an inch. When the asphalt has hardened and thoroughly cooled (two to three hours or longer), the clay walls are to be removed, and the whole preparation washed. Examine it carefully all round, to see if there are any uncovered points. If so, a little fresh asphalt may be run in or the part touched with a hot spatula.

The preparation is thus included in a perfectly air-tight chamber, and no further trouble will be experienced with it, provided it is not kept in too warm a situation or in the direct sun's rays.

If it is desirable to show both sides of the preparation, each, of course, requires to be polished in the freezer; but if this is not desirable, the back of the slide on which the preparation is mounted is to be coated with "Brunswick black," and the sides of the cell, including the asphalt and the edges and back of the slide, are finally to be covered with paper. It should now be framed and hung in a good light on a wall, or placed in a case in the museum.

31. **Giacomini's Method for Preserving Brain.**—This is a method for preserving brain in an entire state so that it may be utilised as a hand specimen. It is useful merely as a means of showing the exterior. It is not suited for demonstrating the cut surface of internal parts.

The procedure (No. 26, 1878; and No. 5, xiii. p. 282) consists of two stages. In Stage I. the brain, obtained as fresh as possible, is immersed in saturated solution of chloride of zinc. It floats with the surface slightly above the fluid, and must, consequently, be turned several times daily, in order that every part may come in contact with the fluid. If the subject has been dead for some time, 600 grms. of the liquid are injected through the carotids, under slight pressure, and before the organ has been removed. This renders the organ somewhat firm, so that it can be handled with less danger of injury. In forty-eight hours the membranes are to be taken off, and while doing so the brain should be kept floating in the liquid or in water. It is allowed to remain in the solution until it begins to sink, but no longer, and is next immersed in alcohol for ten to twelve days. Here the first stage ends.

Stage II. consists in soaking the brain in glycerine, to which may

be added 1 per cent of carbolic acid. It floats at first, but as the glycerine is imbibed, it gradually sinks. It is now set aside for several days until the surface becomes dry, and is subsequently protected from dust and injury by a coating of gum elastic varnish or marine glue diluted with alcohol.

32. **Gelatine-Potash Method for Preparing Large Naked-eye Sections of Brain.**—This process was formerly published by the author in "Brain" for July 1883. Since then, however, several important modifications have been made in it, which are included in the present description. It is specially recommended for the study of the normal brain and for that of all morbid brains where the lesion is perceptible with unaided vision.

(*a*) *Hardening.*—The brain is to be hardened by injecting it with Müller's fluid in the manner recommended in Chapter V. When it has become sufficiently tough (two to three months) it is cut into slices of such thickness that they will easily get into the well of the large freezing microtome (Sect. 39). They should be as thick as possible, as in this way there will be fewer breaks in a continuous series. They must not be placed in spirit of any description. The thick slices are laid, without being freed from the Müller's fluid, in "B" freezing solution (Sect. 37), and are retained in this permanently. They must not be cut for at least a fortnight after being immersed in it, and are all the better for being left much longer.

(*b*) *Cutting.*—Sections are next cut from them in the large microtome, in the manner detailed in describing it, great care being taken, while freezing, to brush the surface with mucilage, and to pad the space between the *front* of the segment of brain and the microtome with freezing fluid "A" (Sect. 37). Gum does not suit for this purpose, as it forms too hard a mass to cut through and is liable to split. If the section, instead of landing in the basin in front, sticks to the blade, it is not sufficiently frozen, and more snow and salt must be placed in the freezing box and firmly packed under the stage. It should perform one revolution and land on the surface of the liquid, if everything is working properly. If this were not so, nearly every section would be mutilated in endeavouring to spread it out. If it curls up in the liquid, it should, when it has thawed, be unfolded, with two large camel's hair brushes.

The liquid to be placed in the trough in front for the purpose of receiving the section should not be water, but a syrup whose specific gravity is as great or greater than that of the freezing fluid in which it has been soaked. If water is used, the section will swell and become irregular.

(*c*) *Embedding in Gelatine.*—Before cutting the section a piece of common window glass without flaws, 12 by 11 inches in size, is covered with a solution of gelatine made by steeping French gelatine in water for ten minutes, melting it, and adding an equal bulk of water with sufficient carbolic acid to raise the whole up to a 1 to 40 solution. The

carbolic acid should be thoroughly dissolved in the water before being added. The best way to spread the gelatine over the plate is to pour it on rapidly with a large pipette. This gelatinised plate, when the gelatine has set, is moistened under a running stream of water. All air-bells, which may be adhering to its surface, are to be removed, and it is subsequently to be placed in the bottom of the trough, immersed in the sugar solution. As it is somewhat difficult to catch hold of the glass plate when it rests directly upon the bottom, it is well to separate them by two small pieces of glass.

The cut section usually floats on the surface of the liquid. The plate of glass is now lifted up with the preparation upon it, and is set aside in a gently sloping position for half an hour or so, until all the superfluous liquid has run off, and until the section has become slightly sodden. If successfully accomplished, the position of the parts ought to be exactly that which they had before being cut. Where a series is being cut they should be laid down in regular order, but it is not necessary to label them as yet. The same gelatine solution as that before described is now dropped on to the section and for about an inch round it, at a pretty high temperature. The higher the temperature, provided it has not actually reached boiling point, the better will the one layer of gelatine become incorporated with the other. The section has now been enclosed above and below in a gelatine casing, and is free from much chance of being injured.

The preparations are next labelled and left exposed to the air until the gelatine and enclosed brain are perfectly dry and transparent. This usually requires from three to four days, depending upon the temperature at the time. They should never lie in the direct rays of the sun, or too near any other source of heat.

When thoroughly dry the label is smeared with lard to prevent it coming off, and the plate with the section adhering to it is immersed in a bath of 1 part Liquor Potassæ (Phar. Brit.) and 2 parts water, where it is to soak for from one to two hours. After this the plates are removed and turned up so as to allow the extra potash solution to run into some suitable vessel. With a sharp small-bladed knife an incision is made into the gelatine all round the section at a distance of about 1 inch from the side. If it has been soaked long enough, the preparation should now strip off with very little traction. If it does not, then it must be returned to the solution of potash, and on no account should it be attempted to forcibly drag it off. The surrounding gelatine which has not been required may be washed in a running stream of water and utilised in making glycerine jelly.

The preparation is next laid on the back of the slide and allowed again to dry, being frequently turned so as to prevent it adhering. When dry, a piece of *uncoloured* thin twine is passed through an eyelet inserted in the surrounding margin of gelatine, with a label affixed to it, indicating the particular series to which it belongs and the number in that series.

So far, the preparation is perfectly safe and can be kept indefinitely in this dried state, until such time as it may be convenient to expand and mount it.

(*d*) *Stretching.*—The gelatine, on account of the potash it contains, has now become so hygroscopic that if placed in water it will expand to nearly double its size, and, at the same time, the contained section will be stretched to a corresponding degree. As the water rushes in it also differentiates the gray from the white matter in a most remarkable manner.

Water may be employed as the expanding agent, but Müller's fluid is preferable. It is preferable because it cannot expand the preparation too much nor irregularly; it defines the gray and white matters better; and lastly, but not of least importance, it removes any insoluble deposit which may have been thrown down in the gelatine. The sections ought to be left in a flat porcelain trough for a night thoroughly covered by the Müller's fluid, the labels being allowed to hang over the side. They are afterwards placed in a running stream of water, until all trace of the Müller's fluid has vanished. The supply of water should be free, and where a number of preparations are lying together, their position should be altered from time to time, so as to get rid of the colour as soon as possible. It usually requires about two hours; and as soon as this has been done they are laid in a mass on a sloping surface so as to drain off as much of the water as possible.

(*e*) *Mounting.*—They are next immersed again in the mixture of Liquor Potassæ and water (1 to 2) and allowed to remain for about an hour and a half. The greatest care, however, should be exercised, that they do not remain beyond this, as the gelatine will become softened and the preparation so ruined. What is required is to get the exquisite transparency which this procedure occasions. As soon as this is obtained they are to be withdrawn on a clean sheet of glass. The tie-label is now cut off, and, as the preparation is to be permanently mounted on this slide, a fresh one is gummed on to one of its corners. The slide is placed in a sloping position; and as soon as all the extra liquid has been removed, the preparation is covered with the following glycerine jelly dropped on at a low temperature (80° to 90° F.) with a pipette:—

Soak French gelatine in water for ten minutes. Melt in a water bath and to 20 oz. of this add 20 oz. of water. To 40 oz. glycerine add 1¾ oz. liquid carbolic acid, and stir this gradually into the gelatine solution. Filter through sieve cloth.

When the glycerine jelly has thoroughly set, grease the label with lard as before, and place in an alkaline bath having this composition,—

Glycerine	1 part.
Liq. Potassæ (Phar. Brit.) . . .	2 parts.
Add Carbolic Acid in proportion of .	1 to 40 parts.

Allow them to remain for at least twelve hours in this. They take no

VANGIL! ANA!

harm if they are left for twenty-four hours. Remove the slides and place them upright over a vessel suited to catch the superfluous liquid.

With a fine small scalpel cut all round the section, *as close into its margin as possible*, and strip off the surrounding glycerine jelly. Make an acid glycerine jelly by adding half a drachm of glacial acetic acid to an ounce of the jelly just recommended, and with a small pipette, run a narrow margin of this round the edge of the preparation—not over it, but in immediate contact. Allow it to remain for half-an-hour, and subsequently wash off with a large, camel's-hair brush and hot water, taking care that in washing none of the water flows over the preparation. The object of using the acid glycerine jelly is to prevent a white deposit taking place at the margin. For some unknown reason a precipitate always forms in this situation, and seems to be due to an insoluble carbonate. The procedure described effectually prevents it forming, as it sets free the carbonic acid at the margin with effervescence.

Dry the glass plate and next run round the margin of the preparation sufficient ordinary glycerine jelly, to lie beyond the edge of the cover-glass when this is applied, pouring it on until it is at the same level as the surface of the preparation. Let it thoroughly gelatinise, and now the preparation is ready for covering.

With a large, camel's-hair brush moisten the whole surface of the preparation with equal parts of glycerine, water, and carbolic acid up to 1 in 40. Clean another piece of window glass as a cover, considerably larger than the preparation, and brush over the lower surface with the same. With a large pipette pour a quantity of glycerine jelly over the preparation. Allow one edge of the cover to come in contact with it first, and gradually bring the remainder of the cover down over the surface. Hold in position for a minute or so until the glycerine jelly solidifies.

(*f*) *Cementing.*—So far as the mounting of the preparation goes, all is now finished, but a most important part of the *technique* remains to be carried out, namely, the cementing of the edges. The accomplishment of this is more troublesome than any other stage in the process, and out of all the imaginable methods that have been tried there is only one which is effectual. The difficulty is that when the cover is retained with any of the usual cements, the preparation sucks in air, and the cover glass or slide cracks. Some of them hold, but the majority in course of time give way. From these causes many beautiful specimens may be lost.

The method consists in cutting off the superfluous glycerine jelly outside the cover, and in washing the whole slide and cover quite clean. This *must* be done within twenty-four hours. The slide is then thoroughly dried, and a strip of clay is next laid all round the cover glass at a distance of half an inch from its border. Into the trench so formed melted asphalt is poured composed of pitch, sand, and about 1 part of Archangel tar to 8 of pitch. It does quite well

without the sand, but as this increases the bulk and does not destroy the efficacy of the asphalt, it may be added. It is melted in a shallow ladle, such as that employed by plumbers for lead, and is run for a short way over the cover glass as well as into the trench. It solidifies almost immediately, but it is better not to touch it for several hours. The clay is then removed and the slide washed.

(*g*) *Finishing.*—The whole slide should now be neatly covered in with a tinted wall-paper, as this effectually prevents the asphalt from adhering to any adjacent object. Each set of preparations should have a paper of a distinctive tint, and a label must, of course, be affixed.

Such gelatine-potash preparations may be viewed in two ways, either as opaque or as transparent objects. Of the two, the opaque are preferable for the middle third of the brain, that is to say, for the parts about the basal ganglia, but in front and behind this they are better to be transparent.

To make an opaque preparation the back of the slide should be coated with Brunswick black before covering with paper. Some of the preparations mounted in the above method are clear enough to be examined as transparent objects; but if it be desired, for instance, to show the Gratiolet's optic radiation band in the parieto-occipital region, it is necessary to make the sections transparent by the following means:—

(*h*) *Transparent Preparations.*—The process is alike up to the stage at which the cover glass is about to be put on. Instead of covering the preparation at once, as is done when the preparation is to be opaque, it is allowed to dry for a fortnight or three weeks in some chamber protected from dust. The glycerine which it contains prevents it from drying completely, but the water will in great part evaporate and leave the section perfectly clear, in fact too transparent to bring out its best points. It is now, however, brushed over with the glycerine, water, and carbolic acid mixture, and mounted as before. This causes the natural opacity of the white matter in part to return, but so delicately that light easily passes through it.

(*k*) *Concluding Remarks.*—The process may seem complicated to any one reading a description of it for the first time, and the reason for all the stages may not be apparent to one unversed in the difficulties which beset the path at every turning. The reader may be assured, however, that there is a reason for every step in the procedure, and that unless he follows out the foregoing directions to the letter he will certainly meet with disappointment. The result when successful is ample reward for all the trouble.

33. **Vessels for Mounting Preparations.**—Of all *glass preparation jars*, that devised by the late Professor Goodsir seems to be by far the most serviceable. It is a plain round jar with a ground top, to which a glass cover is accurately fitted. A metal band about one-quarter inch wide runs round the edge where the two meet, and effectually prevents the cover slipping. When about to be used the

hollow of the metal band should be filled with lard. The band should then be slipped over the edge, and the superfluous lard removed. The advantages possessed by this jar are that it is very sightly; the lid can be removed at any time, and is easily readjusted; and it has no tendency to crack. The metal band should be coated with Brunswick black to prevent its corroding. There are two little notches within the jar into which a piece of cane should be slipped. The preparation is slung by the thinnest thread, and this is not to be tied to the cane but inserted into slits in its side. The preparation should be hung by two separate threads attached to different parts, as otherwise it is very difficult to turn it when in the liquid.

Flat-sided jars are now common in several museums, and are preferred by many curators. *Basins made of earthenware or glass* are very useful for mounting large preparations such as those of the heart, liver, and lungs, dissections of large vessels, muscles, etc. The preparation is fixed in position by means of plaster of Paris, which is poured in until it rises to the proper level. If the basin is now slightly shaken, the plaster will settle at a uniform level. The cover-glass is made of plate glass, and is very liable to crack with changes of temperature, and, moreover, it is difficult to cement it on to the ground ledge of the jar so as to prevent liquids in course of time oozing out when the jar is inclined. The best cement for the purpose is made of a mixture of gold size and red lead (Symington). The gold size is evaporated down until it becomes considerably thicker than it is naturally, and is then made into a paste with red lead. It hardens within a week, so that the basins can by that time be filled with spirit and inclined at the angle most suitable to show them. The edges of the jar and cover should subsequently be varnished with zinc cement (Sect. 46).

A much better method, however, in order to avoid the difficulty of preventing the liquid from oozing out, is to mount the preparation in glycerine jelly (Sect. 28). This not only fixes the preparation, but, of course, when solid, gives no further trouble.

34. **Painting of Museum Preparations.** — It is sometimes desirable to colour blood-vessels of distinctive tints in a jar preparation in order to catch the eye of the observer. If the preparation is mounted in spirit this can be done very readily by means of ordinary metallic water colours mixed with gum. The preparation should be hung up for a little until any superfluous liquid has run off. The colours are then easily painted on with a sable-hair brush.

Hæmorrhages and other discolorations may thus often be restored to great advantage. If the preparation is mounted in any medium which will dissolve the water-colour, a mixture of oil paint and gold-size will be found useful. Spirit preparations are, however, always the most satisfactory for painting.

CHAPTER V

THE PROCESS OF HARDENING TISSUES

35. We have already (Chap. III.) seen how to examine the tissue microscopically when fresh. In order to proceed to its further microscopic examination, it is necessary to employ some reagent which will render it easier to cut into thin sections, which will make it impervious to media of different densities in which it may be mounted, and which will bring its histological elements better into view. Experience teaches that in hardening pathological tissues only a few reagents are necessary.

36. **Reagents.**—It is very difficult, much more so than in normal histology, to say what media are the best for hardening particular morbid tissues, but the following general rules will be found serviceable as a guide. (1) If the tissue is tough, such as a scirrhous tumour, a cirrhotic liver or kidney, or a myoma; or if it is to be stained with logwood or an aniline dye, harden in spirit. (2) If it is of delicate texture, such as a myxomatous sarcoma, an œdematous fibrous tissue, brain, or spinal cord, place it in Müller's fluid alone, or this, followed in three weeks or so by spirit. Müller's fluid preparations also stain well with logwood. (3) If it be a preparation of the retina, employ a mixture of Müller's fluid and spirit. (4) In a few diseases of the lung, such as emphysema and anthracosis, employ a solution of chromic acid. It will be necessary, however, to mention in detail what individual morbid tissues are to be hardened in when we come to their systematic description, and in order to save repetition, each reagent will be designated by a letter (A, B, C, etc.).

Solution A.—*Methylated Spirit.* This, it must be remembered, is not absolute alcohol, but can be made nearly absolute by the addition of a little dry carbonate of potash.

Solution B.—*Absolute Alcohol.*

Solution C.—*Müller's Fluid.*

Potassic Bichromate . . .	grm. 45.
Sodic Sulphate	grm. 20.
Water	2 litres.

Solution D.—*Müller's Fluid and Spirit.*

Müller's Fluid	3 parts.
Methylated Spirit	1 part.

(Allow it to cool before using.)

Solution E.—*Chromic Acid.* $\frac{1}{4}$ to $\frac{1}{6}$ per cent.

Solution F.—*Chromic Acid and Spirit.*

Solution of Chromic Acid ($\frac{1}{4}$ per cent)	3 parts.
Spirit, ...	1 part.

(Keep from the light.)

Solution G.—*Perosmic Acid.* ($\frac{1}{4}$ to $\frac{1}{8}$ per cent.)

Solution H.—*Gold Chloride.* ($\frac{1}{2}$ to 2 per cent.)

Solution I.—*Picric Acid.* Solution saturated in the cold. Hardens in a few days. If the tissue is left longer it becomes brittle.

Solution K.—*Decalcifying and Hardening Solution* (*Rutherford*).

Chromic Acid	1 grm.
Water	200 cc.

Then add 2 cc. Nitric Acid.

In the *Journal of Anatomy*, vol. xii. p. 254, the author recommended a mixture of Müller's fluid and spirit for hardening brain and spinal cord. It is a very good medium where these have to be examined microscopically, but it will be found that for making large preparations according to the gelatine-potash method pure Müller's fluid is preferable. The author formerly (No. 9, xv. 1875, p. 335), used the mixture of chromic acid and spirit (F) pretty freely for nerve and other tissues, but of late has almost completely given it up. It is a good hardening fluid for some lung specimens, but it should be remembered that it is extremely liable to decompose, and must be changed frequently. It is useful where it is desired to harden a tissue rapidly, but its use should not be continued beyond eight to ten days, otherwise the tissue will refuse to stain with many of the most useful reagents. The hardening may be completed in methylated spirit.

All chrome-salt hardening reagents, and the chromic acid and spirit mixture, should be kept in the dark, otherwise the light will rapidly decompose them.

Method.—The best jars for the purpose are those made of earthenware, with an earthenware lid and an iron clamp. They are cheap and very strong, so that they seldom get out of order. They are also the best for retaining pieces of tissue when they have been hardened.

A piece of old washed linen rag is placed in the bottom of the jar, and the latter is three-quarters filled with the hardening liquid. Two or three pieces of the tissue, cut into $\frac{3}{4}$ to 1 inch cubes, are placed within the jar, and covered by a second piece of linen. Another layer of tissue is placed above, and so on until perhaps three or four layers have been built up. The liquid, if it be spirit, or a solution of a chrome salt, must be changed on the following day, and perhaps once or twice

afterwards. Any blood which may be at the bottom of the jar is to be removed, and the position of each piece of tissue altered. As a rule, it will not be found necessary to change methylated spirit oftener than three times, and twice is usually sufficient. Müller's fluid should be changed at least three times, a good deal depending upon the amount of blood in the tissue; and a large quantity should always be employed. The Müller's fluid and chromic acid combinations with spirit (D and F), require renewing oftener than any other hardening fluids, especially if exposed to the light.

Hardening of Brain.—The brains of small vertebrates are best hardened by placing them simply in Müller's fluid for such time as is necessary to render them tough, and, subsequently, for a very few days in methylated spirit.

Where we have to do with the human brain, however, the following method will be found the best. It is suited for the preparation of the organ where it is required for naked-eye dissection, where it is intended for gelatine-potash preparations (Sect. 32), or, lastly, where it is desired to use it for microscopic investigation. Microscopic sections made from an organ so hardened can be stained with most reagents, and more especially is it suitable for Weigert's method of hæmatoxylene staining (Sect. 43, II.).

A brain hardened in spirit is a brain spoiled. All differentiation between white and gray matters is lost, and the organ becomes so shrunken and deformed that it is quite useless for further investigation. The only objection to the following method is that it occasionally makes the organ a little too large, but in no case, if properly carried out, does it alter its proportions or cause distortion.

In removing the organ, saw through only the outer table of the skull, and chip the inner across with a chisel and mallet. Cut round the dura mater as usual with a probe-pointed bistoury, taking the greatest care not to wound the brain substance. Dissect as much of the internal carotid arteries out of the canals as possible, and cut the vertebrals very long. Remove the organ from the skull in the usual manner.

A bulky round earthenware basin with an earthenware lid must be in readiness, as the hardening is to commence at once. Fix a large-sized cannula into each of the internal carotids and tie it in with thin waxed twine. Fix another similar cannula into one of the vertebrals tying the vertebral opposite. Previous to fixing the cannulæ into the vessels, attach a piece of strong rubber tubing to each of the former, a foot and a half long. See that this is done *before* tying them into the vessels, as it is difficult to do so afterwards. Place the brain, with the three cannulæ inserted in its vessels in the round earthenware basin, and in order to take the weight of the cannulæ off the vessels, allow the tubes to hang over the edge. Fix the rubber tubes to the connecting tubes represented in Fig. 12 (*b*,*b*,*b*). The common tube (*a*) is in communication with a tank, which can be elevated or depressed.

Into the tank a large quantity of Müller's fluid is poured, and it is elevated to a height of about 4 feet. The stop-cock attached to the tank is gradually turned on, so as to allow the Müller's fluid to percolate slowly through the organ. In order to give the fluid free play care should be taken to place the cannulæ in the natural direction of the vessels, and to see that their points are not pressing upon the walls.

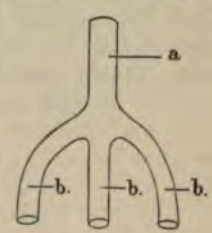

FIG. 12.—BRASS TUBES FOR CONNECTING INJECTING TUBES WITH THE TANK OF MÜLLER'S FLUID.
(*a*) Main Stem; (*b,b,b*) Tubes to be attached to those coming from the Cannulæ.

The first Müller's fluid which flows out contains blood, and should not be again employed, but the subsequent injections can be made with the same Müller's fluid over and over again. It usually runs through very quickly, and the tank should be replenished at least every day for a week or oftener if it is found convenient.

The brain should be always freely supported by an excess of Müller's fluid, and there should be an overflow vessel into which the waste may escape. The fluid should be capable of being removed from this vessel without disturbing the brain or the position of the cannulæ. If the tank is replenished daily for a week it is usually sufficient, but, if convenient, the injection may be continued for a fortnight. The longer it is continued the better will the organ be hardened. It may be finally left in the Müller's fluid for from two to three months, or even longer. The organ is not injured by time, and some of the most beautiful brains will be found to be those which have been in the Müller's fluid for five or six months. The hardening process must not be hastened if thorough success is desired.

While hardening, it should not be padded to keep it in position. The best means of retaining its proper contour is to leave it in a plentiful excess of the liquid, and its position should be occasionally changed. When cut into, after being completely toughened in this way, it presents a truly beautiful appearance. If the segments are to be used as naked-eye objects they ought to be treated in the manner described in Section 30.

If they are to be employed in making *gelatine-potash* preparations, the segments should not be hardened any further, but if they are to be frozen in order to cut *microscopic* sections the pieces should be left for three days in methylated spirit once changed. The spinal cord and medulla oblongata when hardened in Müller's fluid alone, cut excellently with the freezing microtome. The brain cortex cuts beautifully also when hardened in this manner, but the freezing fluid acts upon the tissue in such a way that it shrinks the cortical nerve cells and neuroglia, and leaves a wide space round the former. This can be obviated by placing the pieces of brain, hardened as above, in spirit, for three to four days according to their dimensions. The pieces should not be beyond half an inch in thickness.

Preparation of Hardened Tissues for Cutting.

37. Since the introduction of the freezing microtome by Rutherford, the cutting of sections of hardened tissues for microscopic examination has become very much easier than before. Every pathologist should provide himself with one or more freezing microtomes, one for ice and another small simple one for ether, or one in which these are combined. There is practically no pathological tissue which may not be cut in a freezing microtome. The ease with which it can be done, as well as the beauty of the resulting sections, are unsurpassed by any other method. The whole secret of freezing a tissue and cutting it without injury to its structure consists, however, in knowing how to prepare it for freezing. Those unacquainted with these methods, constantly assert that it is necessary to embed such and such a tissue in paraffin, wax, or some other such mixture, as it is unsuitable for cutting in the freezing microtome.[1]

The matter is so simple that the briefest instructions will suffice. It is only in certain cases that embedding is required; and even when embedded, the tissue can always be cut with the freezing microtome, using the embedding medium merely for the purpose of holding the section together so as to prevent its becoming injured by handling.

If a tissue has been hardened in *spirit*, the first thing to do is to soak it in running water for twenty-four hours. If it has been hardened in a chrome salt or in chromic acid, do likewise, unless in the case of the brain or cord when Weigert's method of logwood staining is to be adopted.

The hardening fluid having been removed by the running water, the tissue has next to be placed in one of the following *freezing fluids*:—

Make a syrup of the strength of 28·5 grm. of pure sugar to 30 c.c. of water. While the syrup is boiling, saturate it with boracic acid. Filter through muslin when cold. Make a mucilage of gum acacia in *cold* water of the strength of 45·6 grm. of gum to 2400 c.c. of water. Saturate with boracic acid by boiling, and filter as before.

Freezing Fluid A.

Take of the syrup	. . . .	4 parts
" mucilage	. . . .	5 "
" water	. . . .	9 "

Boil and saturate while hot with boracic acid. Filter when cold through muslin.

[1] The great objection to freezing delicate tissues is that they become marked by the crystals of ice, and are thus totally unfitted for microscopic observation. In some of the German laboratories they have lately almost given over using the freezing microtome on this account, and are employing ponderous and expensive machines, with results anything but satisfactory.

Freezing Fluid B.

Take of Freezing Fluid "A"	.	2 parts
" syrup	. . .	1 part

Freezing Fluid C.

Take of syrup	. . . .	4 parts
" mucilage	. . . .	5 "

These three fluids freeze with different degrees of hardness. That marked "A" freezes very easily; that marked "B" is more difficult to freeze; while that marked "C" just freezes, but with considerable difficulty, a very low temperature being necessary.

According to the *delicacy* of the tissue, it ought to be placed in one or other of these fluids before being cut. For by far the greater number of tissues, the "A" fluid is sufficiently strong, but it may happen that we have to do with a very delicate structure and one which cannot be hardened to any great extent without being spoiled. In such a case the "B" fluid should be preferred; while very exceptionally it happens that in order to prevent the ice injuring the tissue it is necessary to employ the "C" freezing fluid. This, however, is rare.

The time required to soak the pieces of tissue varies according to their size and other circumstances, such as the presence of adipose tissue round them. It is always safe to give a week's time with any of them.

Instead, however, of merely soaking portions of the tissue as they are required, it is much better to keep all hardened tissues permanently in the fluid. The longer they are kept the better, for, as time goes on, the piece of the morbid organ or tumour, as the case may be, becomes saturated with the solution in every part, and cuts without any tearing or irregularity. It is often said that the freezing microtome tears the sections. Such a libel is unjustifiable; should the tissue be injured, it is owing to its having been imperfectly soaked with a proper *freezing fluid*.

The next thing to be done, therefore, after the hardening fluid has been got rid of, is to put the piece of tissue in a stone-ware jar with sufficient freezing fluid of either of the three strengths to cover it. Put a label on the jar with a number corresponding to a duplicate in a catalogue. The jar may be filled with different organs and tissues, provided that they are of sufficiently distinctive appearance to be recognised. Thus pieces of kidney, liver, lung, and a tumour may be retained in the same jar, if the label outside states distinctly what is in it, and refers each to the number of the jar kept in the catalogue. In this way much space is saved, where many tissues have to be stored. The convenience of having each of these in a state fit for freezing at any time will be readily appreciated.

It is well to place every tissue first in the "A" fluid and to freeze a piece in order to see whether the solution is strong enough. If it is found that the tissue has been injured by the ice, soak another

piece in the "B" fluid, and usually there will be no difficulty in cutting it in perfect preservation. If a tissue has been overhardened it sometimes falls to pieces when cut, after being soaked in the "A" fluid. If so, try the "B" fluid, and, in all probability it will cut much better.

Methods of Embedding.

38. As a rule tissues ought not to be embedded in any basis if it can be dispensed with. It occasionally happens, however, that when cut and placed in water, the parts may become detached and thus their relationship will be lost; or the tissue may be so easily broken, that it is almost impossible to stain and mount an entire section. In such cases it is advisable to embed in some medium before freezing, and it will depend upon the medium employed whether this should be done before soaking in the freezing fluid or afterwards.

The Celloidin Process.—This procedure will be found excellent for brain, spinal cord, and many other organs. The spinal cord usually cuts perfectly when it is simply allowed to soak in the "A" solution after being hardened in Müller's fluid. With the parts above this, however, there is more difficulty, and with the hardened cortex the difficulty of cutting in a freezing microtome is extreme. The following method of embedding and soaking, however, makes the cutting of any portion of the brain a matter of the greatest ease :—

Harden the brain in Müller's fluid as before described, and cut the part to be examined into slices from one quarter to half an inch thick. Place these in methylated spirit for three to four days, changing daily. Transfer them for two days to a mixture of equal parts of absolute alcohol and ether. Make a thick solution of celloidin[1] in equal parts of ether and absolute alcohol. It should resemble a thick syrup when of proper strength. Place the pieces of brain in this, and allow them to remain for at least four days, until the dissolved celloidin has thoroughly soaked into them. Make a paper boat, or, what is as good, use a pill box, and, placing the piece of tissue in this, fill it with the celloidin solution. Allow it to stand exposed until it partially hardens. A crust of hardened celloidin forms on the surface in about half an hour, but the time required will depend upon its bulk. Complete the hardening of the celloidin in methylated spirit. Twenty-four hours is necessary to accomplish this.

The piece of brain is now surrounded by a hard horny mass of celloidin of a slightly milky translucency. In order to prepare the embedded tissue for freezing, it must be soaked for twenty-four hours in water and be subsequently permanently kept in the freezing fluid "A" or "B." It is then ready for cutting. The freezing fluid will penetrate much more thoroughly and quickly if the tissue immersed in it be retained in a warm chamber at a temperature of 100° Fahr. for several days.

[1] This can now be obtained directly or indirectly through any druggist.

Gelatine and Freezing Fluid Embedding Mixture.—Where it is undesirable to apply spirit to a tissue, a mixture of 10 per cent gelatine in freezing fluid "A" should be substituted. This will be found to be unsuitable for brain, as the gelatine seems to swell when frozen, and destroys the delicate brain substance; celloidin is preferable. The tissue, such as an embryo or a portion of a stomach, is first stained in mass in carmine or some other staining reagent. It is next thoroughly freed from this by soaking in freezing fluid "A" with frequent changing, and is now ready to be transferred to the gelatine and freezing fluid "A" mixture in a stopper-bottle. In order to allow the gelatine mixture to thoroughly soak into every part, it is kept in a warm chamber at a temperature of 100° Fahr. for several days. The whole mass is subsequently allowed to cool in a beaker. When thoroughly gelatinised, the beaker is placed for an instant in hot water, and the gelatine, so loosened from its hold on the beaker, is removed. The embedded tissues are now cut out, still surrounded by a block of the medium, and are subsequently placed in freezing fluid "B" and retained permanently in this. If this freezing fluid is too strong, that is to say, if there is difficulty in freezing the tissues soaked in it, they should be transferred to "A." For embryos and such like delicate tissues, however, the "B" fluid will be found best. The sections are of course made in the freezing microtome.

As before said, the above gelatine medium is unsuitable for embedding brain, but for many other purposes nothing could be more beautiful. It is superior to celloidin, paraffin, or wax in that the tissue can be transferred directly from water without having been previously subjected to the action of spirit, ether, oil of cloves, or other reagent which might act deleteriously upon it.

Embedding in Paraffin.—As a rule paraffin is inapplicable as an embedding medium for morbid tissues, unless where the "rocking microtome" is employed. Its chief advantage is that ribbons of sections may be obtained by its use, which are kept in proper serial order by adhesion of the one to the other. It is only for very small bodies such as embryos that it can be recommended, and even these, if it is desired, can be cut in serial succession by the method detailed in Section 39.

Stain the body first *en masse* in borax-carmine or some other penetrating reagent. When this is completed, the superfluous staining fluid is washed out in water. The tissue is now transferred to absolute alcohol, and from this to oil of cloves. The oil of cloves should be allowed to act upon it until all the spirit has been removed, the proper stage being known by its becoming transparent, or at any rate by its losing its natural opacity.

A little paper boat is now prepared, and into it is poured some melted paraffin. The paraffin is allowed to cool, and the body to be embedded is laid upon it. More melted paraffin is dropped from a pipette upon the body until it is thoroughly covered in.

If it is desired to make the paraffin harder, colophony resin may

be mixed with it, and if softer and more transparent it may be combined with vaseline (2 to 1). By the latter means the position of an embryo may be observed in the mass, but when the ordinary opaque paraffin is used the position of the embryo should be marked by a pin being inserted into the paraffin at the head end.

Embedding Mixture for grinding Bone, Tooth, etc.—A capital mixture suitable for this purpose is employed by Nicholson in mineralogy. It consists of 2 parts colophony resin and 1 part wax. These are melted together, and the piece of bone or tooth is embedded in the mixture on a piece of glass. It is first rubbed down roughly upon sandstone, and is subsequently polished with emery powder of different degrees of fineness on plate glass.

SECTION-CUTTING.

39. As before stated, all pathological tissues may be cut in the freezing microtome, and in choosing one the pathologist should be guided by its efficacy, durability, and price. Rutherford's, with the author's adaptation of a glass top, is one of the simplest. It should be furnished with a planing iron blade.

Rutherford's Ice Freezing Microtome.—It consists of a hollow brass cylinder fitted with a brass plug capable of being moved up and down by a finely-graduated screw placed below. The handle of the screw should be in the form of a cross bar not of a milled head. The plug ought to be roughened on the upper surface, and a small brass knob is usually made to screw into it, so as to catch the mass of ice and prevent its becoming detached. So far, the microtome is essentially that of the late Mr. Stirling, curator of the Edinburgh Anatomical Museum. Outside of the brass cylinder is placed a freezing box, which should be of large size, and provided with an escape pipe to allow the superfluous water to drain off. Different sizes of cylinder are made according to the dimensions of the piece of tissue to be cut—that which is most useful being $1\frac{1}{4}$ inch in diameter, while a larger one 2 inches in diameter is also to be had.[1]

The whole instrument is surrounded with a thick sheet of gutta-percha, and a plate glass top is fastened on to the cutting surface by cement and a couple of screws.

When the instrument is about to be employed, the plug is withdrawn, the interior of the hollow cylinder is smeared with glycerine, and a little glycerine is poured upon the screw. The plug, previously thoroughly dried, is placed in position and screwed down to the necessary depth, which should always be at least half the depth of the cylinder. A freezing mixture of snow or finely-pounded ice and salt is

[1] Mr. Gardner, surgical instrument maker, South Bridge, Edinburgh, makes these microtomes, but they can also be had from many different firms. Of the two, the larger one is perhaps preferable, although not so handy for small objects, as it can be used for cutting different-sized sections and is provided with a more capacious freezing box.

now placed in alternate layers in the freezing box, and vigorously stirred with some suitable instrument. The salt is apt to accumulate at the innermost part of the freezing box, and must from time to time be cleared out. The drainage pipe of the freezing box must be closed with a cork. The freezing will proceed very much quicker if this is attended to, and the object frozen can be left for a greater length of time, without renewing the mixture, if the liquid is retained. It should be allowed to escape only when it becomes excessive.

When the temperature of the plug has been reduced to freezing point, which may be ascertained by touching it with a damp finger, sufficient mucilage (Phar. Brit.), is poured into the cylinder to form a layer about one-eighth of an inch deep. This is allowed to freeze before putting in the piece of tissue. The latter, taken out of the freezing fluid, is now placed in the cylinder with a pair of dissecting forceps, and held in position until it adheres to the side of the cylinder. It should always be held in contact with the side of the cylinder farthest away from the operator. The tissue is surrounded, lastly, with mucilage, and a piece of strong waterproof texture of any kind, covered by a weight, is put over the mouth of the cylinder to prevent the freezing mixture accidentally entering.

The best blade to employ is that proposed by Delépine, and consists of an ordinary planing iron set in a wooden handle. Nothing could be more efficacious than this knife, and as its cost is so insignificant, several of them may be at hand, ready for use, although they require to be sharpened only very seldom. The handle is held firmly in the palm of the right hand, and the blade is pressed closely down on the glass plate of the microtome at an angle of something like 45°. With the left hand the tissue to be cut is screwed upwards, while the blade is kept continuously playing over the surface. As many as fifty sections may be cut in a single series, and as they are cut they accumulate on the back of the blade. They are afterwards transferred to a basin of water and allowed to unfold. With very delicate tissues, such as brain or spinal cord, it is better to cut each singly; but with liver, kidney, lung, etc., a huge mass of them can be swept off continuously without injury. As many as from two hundred and fifty to three hundred sections may be cut in a minute by this means, all of exquisite delicacy and uninjured.

Rutherford's Ice and Ether Freezing Microtome.—Professor Rutherford has further adapted the preceding instrument for freezing with ether, by which means it has been rendered doubly serviceable. The price, moreover, is less than that of two separate microtomes. When used with *ether spray*, the instrument is arranged as shown in the woodcut (Fig. 13). The tissue, which should not be more than a third of an inch thick, is laid on the zinc plate (Z) and covered with gum. Ether, which must be anhydrous, is then blown from the bottle (O), by the elastic bellows (N), against the lower surface of the zinc plate. Any ether which may escape volatilisation flows down

through the tube (P), and is collected in a vessel. The spray-producing tubes (T) can be readily pulled out of the slit under Z for examination. The tissue is soon frozen, and it remains frozen for about five minutes in a cool room, without any further production of spray.

When used as an *ice freezing* microtome the glass plate L is unscrewed. The supports M and M′, the tubes T, the bottle and bellows, are removed; Z is unscrewed, and the plug K screwed in its place, and sunk deep in the well. The glass plate L is then screwed on the brass plate B, and the instrument is ready for use. The further particulars are of course the same as in the description of the simple ice-freezing instrument.

FIG. 13.—RUTHERFORD'S ICE AND ETHER FREEZING MICROTOME.

Large Ice Freezing Microtome for Cutting Sections of an Entire Organ.—Mr. Gardner of Edinburgh has constructed, from the author's designs, a large microtome for cutting sections of entire organs such as brain, liver, or kidney. It is built essentially on the same principle as Rutherford's ice instrument, but the blade, instead of being held in the hand is fixed in a ponderous framework which runs in a railway placed on each side of the stage. The framework for the blade requires to be very heavy so as to gain the necessary momentum, and the blade should be made like a planing-iron, but of particularly thick steel, so as to prevent its bending when it catches the edge of the frozen tissue. The freezing mixture is composed of snow and salt;

and care must be taken, as in the former, to close the escape tubes by corks, otherwise a long time will be required to freeze the object completely over. If properly carried out, a piece of tissue three quarters of an inch thick ought to be frozen, in from twenty minutes to half an hour, according to the temperature of the room.

The interior of the cylinder and the screw are anointed with glycerine as before, and the brass plug is placed in position. When reduced to freezing temperature, a quantity of mucilage is poured over the plug, and the organ to be cut is placed directly in this to the depth of about a sixteenth of an inch. As the freezing goes on, the outside of the organ is brushed with mucilage, and the space between *the front* of the organ and the well of the cylinder is to be gradually

FIG. 14.—LARGE MICROTOME FOR CUTTING SECTIONS OF AN ENTIRE ORGAN.

filled up with freezing fluid "A." In order to accomplish this fix on a thin slice of jelly, made from French gelatine, at each side; allow it to become frozen; and afterwards fill the enclosed space with the freezing fluid. The whole well should not be filled with freezing fluid, as this is unnecessary. The pad formed by that placed in front is quite sufficient to support the preparation.

The blade is driven forwards evenly and rapidly, great care being taken that the railway is thoroughly greased with a mixture of olive oil and glycerine. The section is thrown off from the blade, and lands on a trough filled with water or other suitable liquid placed in front. It should never adhere to the blade if properly frozen. With a huge mass of ice, such as an entire brain represents when frozen, a great deal depends upon its consistence. It may be too much or too little frozen, and practice alone will tell the operator what is the necessary point to attain. If thoroughly soaked in "B" freezing fluid, however, it is almost impossible to freeze too hard.[1]

[1] Dr. Bruce has devised a large freezing microtome for similar purposes made by Mr. Frazer, 7 Lothian Street, Edinburgh, the chief difference between it and the author's being that the blade is movable instead of the brass cylinder on which the segment of tissue is fixed.

Williams' Microtome.[1]—This consists of a round waterproof box of large size for holding the freezing mixture, in whose centre an upright brass column is placed which acts as an extractor of heat from the tissue. To the top of this brass column is screwed on a roughened brass disc, on which the tissue is to be laid. A glass plate, with a hole in the centre for the brass disc to project through, forms a lid for the box and a convenient surface for the tripod stand carrying the knife to play upon. The freezing mixture of snow and salt is placed in the box, and when the disc is sufficiently cold, a little mucilage is poured upon it. The tissue is frozen to the disc by means of this, and is from time to time brushed with mucilage during the process.

FIG. 15.—WILLIAMS' FREEZING MICROTOME.

The knife consists of a blade fixed in a tripod stand which is approximated to the tissue, as each section is cut, by means of a finely-graduated screw. This shortens the front leg of the tripod and so brings the blade farther down. The blade is here approximated to the tissue instead of, as in Rutherford's, the tissue being screwed up to the blade.

Lewis' Freezing Microtome.—Dr. Bevan Lewis has devised this little microtome for cutting sections of fresh brain in the process described by him for preparing the cortex. It is useful for other purposes, and it is well to have either this or the following always at hand. Both are adapted for ether freezing; but if anything else than brain is being cut in them, the piece should not be very large. To cut the

[1] Made by Swift of London.

section Dr. Lewis recommends a razor, but the plane blade can also be employed.

Cathcart's Freezing Microtome.[1]—This is also a very serviceable little instrument, and, like the foregoing, is not costly. The plane blade is also applicable for cutting with it. The directions for use are the following:—

(1) Place a few drops of mucilage (1 part gum to 3 parts water) on the zinc plate (H).

(2) Press a piece of the tissue to be cut, about a quarter of an inch in thickness, into the gum.

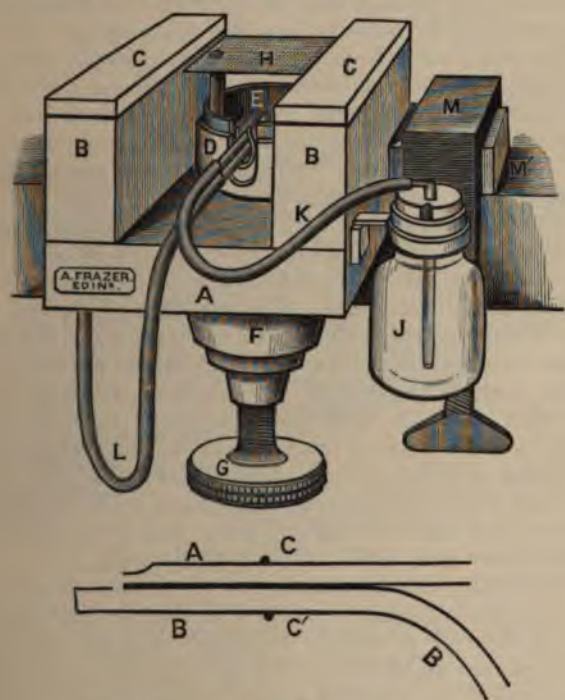

FIG. 16.—CATHCART'S ETHER FREEZING MICROTOME.
Microtome with spray-producer attached; and section of neck of spray-producer.

(3) Fill the ether bottle (J) with anhydrous methylated ether, and push the spray points into their socket (E).

(4) Work the spray bellows briskly until the gum begins to freeze; after this work more gently. Be always careful to brush off the frozen vapour which, in a moist atmosphere, may collect below the zinc plate. If the ether should tend to collect in drops below the plate, work the bellows slower.

[1] Made by Mr. Frazer, optician, 7 Lothian Street, Edinburgh. It costs 15s. complete.

(5) Raise the tissue by turning the milled head (G), and cut by sliding the knife along the glass plates.

(6) After use be careful to wipe the whole instrument clean.

(7) Should the ether point become choked, clear by means of the fine wire which is sent with the instrument.

(8) The instrument is intended for use with methylated sulphuric ether.

Other Microtomes.—Of late years the number of these has become so great that the young pathologist is in danger of getting bewildered by them, and will have some difficulty in knowing whether such complicated and ponderous machines as those of Thoma-Jung, Schanze, and Weigert are really necessary for efficient working. He may rest satisfied, however, that if he is provided with a simple freezing microtome such as one of those just described, for ice and ether, he will be amply equipped. If he buys one of these more elaborate instruments, he will probably resign it in course of time for something much more simple. The great secret of success, as previously remarked, is in the preparation of the tissue for freezing.

How to Cut a Number of Sections in Continuous Series.—Where the object is small and can be embedded in paraffin without injury, probably the best instrument to employ for the above purpose is the "Rocking Microtome."[1] Ribbons of sections can be made with it, each adhering to its neighbour, so that if the series be laid on a long glass slide, they can be mounted in balsam after dissolving off the paraffin with turpentine or oil of cloves, without any further trouble. This certainly is a most convenient method for cutting embryos or such a body as a small spinal cord. It is not well suited for larger pieces of tissue. The Company who make it have improved upon previous instruments of the same kind, by causing the ribbon of sections to fall on to a sheet of paper or a glass slide instead of being carried away with a silk ribbon as previously.

With the ordinary freezing microtome a continuous series of sections may be cut in the following way:—Let us suppose that the tissue to be cut is a piece of a medulla oblongata or spinal cord. Mark a narrow line on the right side of the piece of cord or medulla with gentian violet, and let it remain on for an hour or so in order that it may take a firm hold upon the tissue. Wash in the particular freezing fluid which was employed for soaking. The mark which is left will serve to indicate the right side, however the section may be lying. A shallow four-sided trough ought now to be procured, earthenware is best, divided into a number of narrow spaces from side to side by means of thin partitions. If not specially ordered, this can be easily made if a four-sided photographer's porcelain trough is filled about one-eighth full of melted paraffin, and strips of glass placed in this be employed as the partitions. The strips of glass become fixed in

[1] Price complete £5 : 5s. Made by the Cambridge Scientific Instrument Company, St. Tibb's Row, Cambridge.

the paraffin as it solidifies. The sections as they are cut are dropped in serial order into the spaces formed by the partitions. The spaces should be half filled with freezing fluid or with a staining fluid as may be required.

This in some respects is superior to the ribbon method, in that sections of any size may be cut and retained in order, and can be subsequently stained. They are brought out of the liquid in which they are immersed as required, and placed upon a long strip of glass with the aid of a spatula and camel's hair brush. If they have been in a staining fluid this should first be washed off in a basin of water, and they should then be transferred to freezing fluid. From this they are placed upon the above strip of glass and allowed to get a little

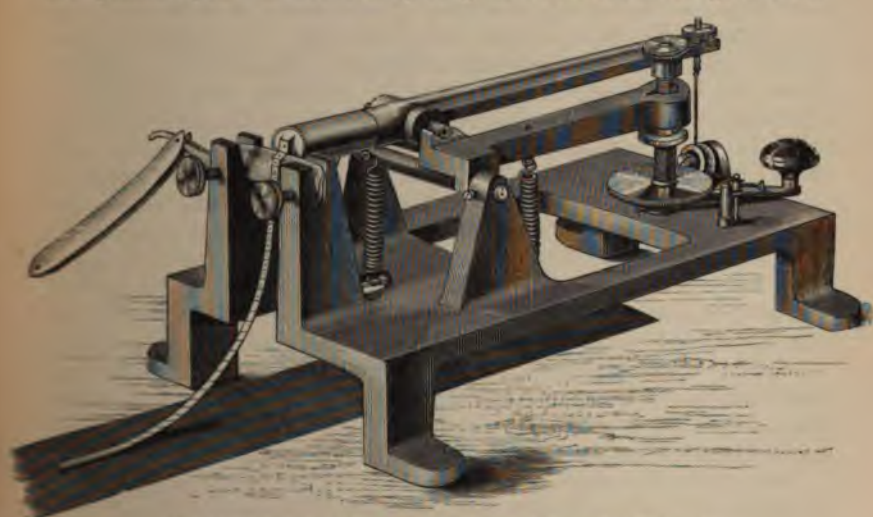

FIG. 17.—"ROCKING MICROTOME" FOR CUTTING RIBBONS OF SECTIONS.

dry. The freezing fluid fixes the sections on the slide, and prevents their moving when the mounting fluid is applied. Farrants' solution is next poured over the series, and they are placed uncovered in a warm chamber. In the course of three days or so, the Farrants' solution will have become hard. They are afterwards mounted in glycerine jelly (Sect. 45), a second strip of thin glass being used as a cover. Immediately after the jelly has solidified, the edges of the preparation are cleaned; and it is secured, firstly, with ordinary glue, and, secondly, after this has dried, with white zinc cement.

Weigert's Method.[1]—This is to be highly recommended, especially for cutting serial sections of spinal cord and medulla oblongata. There are six steps in the process, as follow:—(1) Plates of glass of convenient size (8 × 2 inches or narrower) are covered with a

[1] No. 48, ii. p. 490-494.

thin layer of celloidin solution in ether (collodion is much more convenient, and suits equally as well). They are set on end, and allowed to dry. (2) The second step is to cut the sections and to arrange them riband-wise on strips of transparent (W.C.) paper moistened with spirit, about double the width of the sections. (3) The sections are transferred to the collodion plate by reversing the strip of paper, placing it over the collodion-coated plate, and gently pressing the upper surface. The paper is next peeled off, when the sections will be found adhering to the collodion. Other strips about to be transferred to the collodion plate can be kept moist by laying them upon blotting paper moistened with spirit. No more than one or two strips should be transferred to the same plate. (4) The row of sections is covered with a thin and even layer of collodion, and each series may be marked by a brush dipped in methyl-blue. (5) The collodion-coated glass plate is immersed in Weigert's hæmatoxylene solution (Sect. 43), when it will be found that the collodion separates from it. The rows of sections are thus liberated enclosed in a complete coating of collodion, the whole forming a tough plate which may be handled with impunity. They are decolorised in the manner described in Section 43 and thoroughly washed in water. The celloidin plate may now be cut up so as to separate the individual rows. (6) The rows of preparations are dehydrated in 90 to 96 per cent alcohol and clarified in creasote or xylol.

40. **Preservative Fluid for Sections.**—As a rule, sections, when cut, should not be kept in spirit. They are apt to alter in course of time, and sometimes, as with those of brain and spinal cord, become very brittle. A much better fluid, which seems to act as a perfect preservative, is a mixture of glycerine and water equal parts, with about eight minims of carbolic acid to the ounce.

Any of the freezing fluids do equally well; and if the piece of tissue be small, it may be kept in a bottle along with the sections.

Literature on Section-cutting.—**Barrett** (Section-cutting): J. Anat. and Physiol., xix. 1884-5, p. 94. **Cathcart** (New Ether Microtome): Edin. Clin. and Path. J., i. 1883, p. 473. **Lee**: The Microtomists' Vade-Mecum, 1885. **Nealy** (Rapid Method for Bone and Teeth Sections): Am. Month. Micr. J., v. 1884, p. 142. **Rutherford** (Compound Ether and Ice Microtome): Lancet, 1885, i. p. 4. **Strasser** (Treatment of Serial Sections embedded in Paraffin): Ztschr. f. wissensch. Mikroskopie, iii. 1886, p. 346. **Thoma** (Microtome): Arch. f. path. Anat., lxxxiv. 1881, p. 189.

On Injecting Blood-Vessels.

41. The media employed differ according as it is desired to make an injection for naked-eye or for microscopic purposes.

Opaque Naked-eye Injections.—(1) *Plaster of Paris.* This forms perhaps the best medium for injecting the large vessels of a limb or other such part, where they are afterwards to be dissected out. The plaster of Paris is made thin; and in order to prevent it setting too soon, a small quantity of gelatine or a little alum may be mixed

with the water. The plaster may be combined with various colouring matters.

(2) *Tallow injection* is made by melting tallow and mixing with it sufficient vermilion to give it a red colour. If it is desired to make it a little stiffer, some yellow wax may be added.

(3) *Vermilion and Gelatine.*[1]—A five per cent solution of gelatine may be combined with vermilion, and makes a capital naked-eye injection, finer than either of the foregoing. The vermilion should not be in coarse powder; and in order to ensure that the injection mass is free from large particles, it should be filtered through muslin.

(4) *Yellow Opaque Injection* (Beale).—Cold saturated solutions of acetate of lead and bichromate of potash are mixed. The precipitate is allowed to settle, and the supernatant liquid poured off. The yellow sediment is now to be shaken with warm water and again allowed to settle. It is subsequently added to a 5 per cent gelatine solution.

(5) *White Opaque Injection* (Beale).—Mix saturated solutions of acetate of lead and carbonate of soda in the same way as in No. 4. Treat the precipitate as before, and add it to a five per cent gelatine solution.

It should be remembered that as the gelatine when cold shrinks by being put into spirit, it should not be employed for *large* vessels. These injection masses, it should also be borne in mind, all contain heavy colouring matters, and hence the mixture should be well stirred whenever it is about to be used. Numbers 1 and 2 should be employed for naked-eye purposes alone. Those described under numbers 3, 4, and 5 can also be used for injecting vessels of microscopic size, provided they are to be viewed as opaque preparations. Such opaque injection masses are, however, seldom employed nowadays for microscopic purposes. The following transparent injections are much to be preferred:—

Transparent Microscopic Injections.—The colouring substance of transparent *red* injections is usually carmine, and the best receipt for this injection mass is probably Carter's.

(1) *Carter's Carmine Injection.*

Take of	Carmine (perfectly pure) . . .	1 dr.
„	Strong solution of ammonia . .	2 fl. drs.
„	Glacial acetic acid (50° Fahr.) . .	86 m.
„	Solution of gelatine (1 to 6 water) .	2 oz.
„	Distilled water	$1\frac{1}{2}$ „

Dissolve the carmine in the solution of ammonia and water, and filter if necessary. With pure carmine it is not usually necessary to filter, but it is safe to do so, as carmine is so frequently adulterated. It filters very slowly. The mixture should stand for an hour or two before filtering, so as to ensure that all the carmine will be dissolved. Mix the acetic acid slowly and stir vigorously; then drop the

[1] French gelatine in flakes is the best for all injection masses.

gelatine solution into the solution of carmine, stirring briskly as before. The whole injection mass ought to be slightly acid. A great deal depends upon the purity of the carmine for the success of this injection. It should turn almost black when the ammonia is added to it.

(2) *Blue Injecting Fluid.*—Brücke's blue is very apt to fade when mixed with gelatine, or when injected into a tissue, and it will be found that Turnbull's blue is much faster, especially if combined with oxalic acid. The difference in their composition is that the former is made with ferrocyanide, the latter with ferridcyanide of potassium. Beale (No. 7) gives the following very good receipt. A quantity of oxalic acid is added to the mass, which still further prevents it fading:—

Ferridcyanide of potassium . . .	10 grs.
Sulphate of iron	5 „
Water	1 oz.
Glycerine	2 „
Alcohol	1 drm.
Oxalic acid	10 grs.

Dissolve the sulphate of iron in half the water and half the glycerine in one vessel. In another vessel dissolve the ferridcyanide of potassium in the remainder of the water and glycerine. The two solutions are now mixed, by gradually dropping the iron solution into a bottle containing that of the ferrocyanide and vigorously agitating. The oxalic acid is next rubbed into the mixture in a mortar and the alcohol added. The glycerine causes the precipitate to be thrown down in a much finer form than it is in pure water.

This blue medium may also be employed as a naked-eye injection where the preparation is intended to be hung in a glass jar. When this is the case, gelatine should be combined with it up to the strength of 5 per cent. The gelatine is allowed to lie in it for half an hour, and the whole mass is subsequently melted in a water-bath.

These are by far the best transparent colours. Frey (No. 8) gives the following receipt by Thiersch for a transparent yellow. It requires some care in preparation.

(3) *Transparent Yellow Injection.*—Make a watery solution of chromate of potash in the proportion of 1 : 11 (A), and a second solution, equally strong, of nitrate of lead (B).

Combine 1 part of the solution A with 4 parts of a concentrated solution of gelatine (about 20 c.c. to 80) in a dish. In a second dish, 2 parts of the solution of lead (B) is to be mixed with 4 parts of gelatine (about 40 c.c. to 80).

The contents of both dishes are then to be slowly and carefully mixed together at a temperature of about 25° to 32° C., and with constant stirring. The mass is to be heated to about 70° or 100° C. on the water-bath for a considerable time (half an hour or more), and

finally filtered through flannel. When a dish of this yellow mixture has been kept, it is generally necessary to subject it to prolonged heating, and to filter it again, in order to render it serviceable. Double the quantity of solutions A and B may in some cases be used with advantage.

(4) *Aniline Blue-black Injection.* — One of the finest microscopic injecting liquids is made with *aniline blue-black.*[1] It possesses two advantages, namely, that it is *soluble* in water, and will not transude through the wall of the vessel so as to stain surrounding parts. It may be used simply as a $\frac{1}{4}$ per cent solution in water, or this $\frac{1}{4}$ per cent solution can be combined with 5 per cent French gelatine. The carmine and Turnbull's blue injections are both precipitates, but this being a solution, is of course calculated to run more readily. It does not present such a marked contrast to the foregoing as a brilliant yellow would, but still is quite easily distinguished, and will run into parts which would be impenetrable to carmine or Prussian blue.

(5) *Nitrate of silver* of the strength of $\frac{1}{4}$ per cent may be utilised for injection purposes. It defines the course of the small arteries and veins and the capillaries by staining the outlines of their endothelia. It will act, however, only in a tissue freshly excised from the living subject, or in those of a freshly-killed animal. It should be injected from a glass or vulcanite syringe.

Injecting Apparatus.—(1) *The Brass Syringe.*—Some of the most accomplished injecters have used nothing more than this simple instrument. One decided objection to its use, however, is that there is less certainty of the liquor flowing equably than when continuous air pressure is employed. Another fault is that, as in many other injecting instruments, there is no means for keeping the gelatine warm—a fatal error where the injection is to be driven in slowly. A side tube coming off from the neck of the syringe may be attached to a mercurial manometer (Rutherford), although, with a gelatine injection, this is practically of little use unless the whole tube can be kept under hot water.

The syringe should be well heated in all cases before the injecting fluid is drawn up into it. An injecting mass, further, should always be filtered through muslin immediately before being used.

(2) *Continuous Air-pressure Apparatus.*—Several of these have been recommended from time to time by Ludwig and others. The principle is the same in the whole of them, namely, that the injection is driven in continuously by compressed air. The compressing agent may be mercury or water. Ludwig recommended mercury, but water is more generally employed at the present day. The chief objection to the whole of them appears to be that the arrangements are such that the gelatine mass is not kept heated throughout the entire extent of its course. Some part, sometimes the whole, of the tube leading from the bottle containing the injection is left exposed, and will in a

[1] The particular blue-black can be obtained from Mr. Chaplain, druggist, Wakefield.

few minutes get so cool as to cause the injection to thicken or actually solidify. This is the main cause of gelatine injections proving unsuccessful. The whole gelatine mass and the organ to be injected should be kept at a body temperature during the time the injection is running. The following apparatus is constructed on the usual principles, but is calculated to supply the above want. It can be made out of the simplest materials.

A hollow metal cylinder (Ac, Fig. 18) of two gallons capacity has five stop-cocks fitted into its upper end. One of them is connected to a finely regulated water-tap (T) by a piece of strong rubber tubing

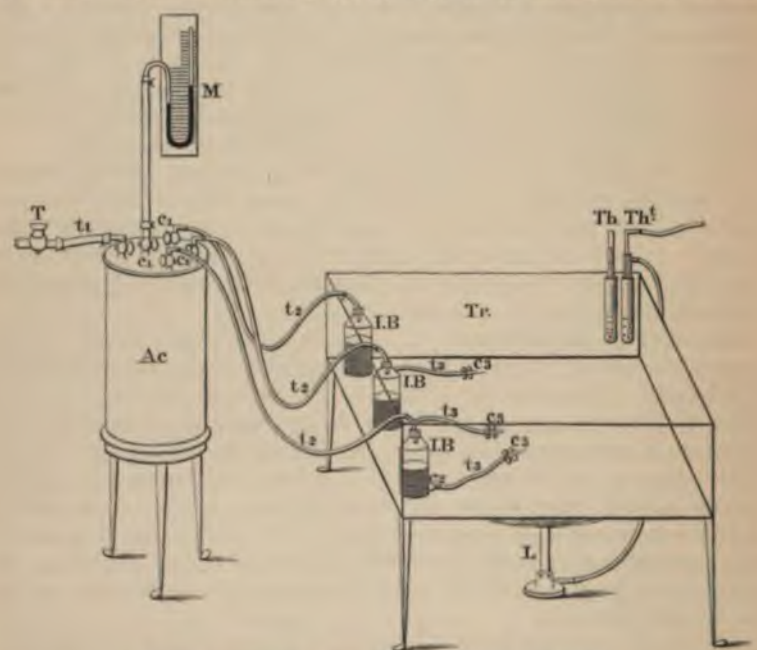

FIG. 18.—CONTINUOUS AIR-PRESSURE INJECTING APPARATUS.

(t_1). Three of the others are attached to the rubber tubes t_2, t_2, t_2, while the fifth is fastened to a rubber tube communicating with a mercury manometer (M). The three tubes t_2 open into a corresponding number of bottles (I. B.) for holding the injection liquids. The injection bottles contain different coloured liquids, and need not necessarily all be used at once. They are made of glass with an opening above and another below, the latter being provided with a stop-cock. The rubber tube t^2 is attached to the upper opening, and that marked t^3 to the lower. To the distal ends of the tubes t_3, t_3, t_3 are attached the cannulæ for inserting into the vessels, each provided with a stop-cock (c^3, c^3, c^3). The injection bottles are placed

in the trough Tr, which ought to have tin sides and a copper bottom. It should measure at least 30 inches long, 18 inches broad, and 8 inches deep, and is to be three-fourths filled with water at a temperature of 100° Fahr. A Bunsen lamp (L) placed below it keeps the temperature from falling, and a most desirable addition is to have the flame regulated by a Bunsen-Meyer thermostat (Th^t). The temperature is indicated by a thermometer (Th). When the apparatus is to be used the injection is allowed to run out of the cannula, and whenever it appears, the stop-cock (c_3) of the cannula is turned and the injection within the latter allowed to solidify. When solid it is inserted into the blood-vessel and tied with waxed silk. The organ with the cannula adjusted is next returned to the trough of water and is kept at a body temperature until heated quite through. All is now ready for making the injection. The tap (T) is turned on until the requisite pressure in the manometer (M) is registered, beginning with half an inch and gradually increasing up to within 3 and 4 inches. When the necessary pressure has been attained, the stop-cocks (c_1, c_1, c_1) are opened, and next those at c_2. Lastly, when the organ is lying in suitable position to allow the injection to flow with least impediment, the stop-cocks (c_3, c_3, c_3) are turned on, and the injection allowed slowly to distend the vessels, the whole organ and injection tubes being meanwhile under water. The organ, when fully injected, will become very tense. When this happens the stop-cocks are to be turned off, the vessels tied, and the organ placed in methylated spirit slightly acidulated with acetic acid.

42. **Injection of Lymphatics.**—A natural injection of the lymphatics of the lung can be made in a very short time by allowing an animal to breathe an atmosphere loaded with paraffin smoke in a confined chamber. The particles of carbon are taken up from the air vesicles, carried into the plasma spaces, and from these conducted to all the lymphatic vessels of the lung and to the bronchial glands.

The usual method is to drive in Prussian blue injection from a subcutaneous syringe by simply slipping the point of the cannula under the capsule of the organ. With most human pathological tissues this method, however, is not very satisfactory.

Corrosion Preparations.—Of late years the method of injecting blood-vessels or ducts of glands with some liquid material which will solidify, and subsequently corroding the surrounding tissues, has been pretty extensively used.

One of the earliest injection masses employed was fusible metal, and for the lung it is still recommended. Plaster of Paris has been utilised for this purpose by Pettigrew and others. The surrounding tissues are removed by allowing the tissue to putrefy and by calling in the services of maggots in summer. The latter soon leave a very beautiful dissection of the injected parts, all that is necessary being to keep the tissue moist.

Schiefferdecker (No. 51 *Anat. Abthl.*, 1882, p. 199), recommends the employment of celloidin. The celloidin is cut in small pieces and dissolved in an equal volume of ether. It can be coloured with different substances, such as pulverised cinnabar or Berlin blue. What is still better, however, is to allow the ether to

stand over asphalt for twenty-four hours, shaking it meanwhile several times. The liquor is decanted and is employed for dissolving the celloidin as before. The solution is injected with a syringe into the vessels, and the syringe is cleaned with ether. The syringe must be free from any fat. The injected organ is laid in hydrochloric acid either pure or slightly diluted, according to the liability of the organ to shrink. When the disintegration of the tissue is complete, its remains are washed off under a gentle stream of water. The injection is so fine that it will penetrate into the vasa afferentia and glomerulus of the kidney. After washing, the preparation should lie in water for a week or two so as to remove any remnant of tissue. It can be kept permanently in glycerine or a mixture of equal volumes of glycerine, alcohol, and water. The most durable mass is that prepared with asphalt.

CHAPTER VI

REAGENTS FOR MICROSCOPIC WORK

43. THESE may be divided into (1) hardening, (2) freezing, (3) staining, (4) clarifying, (5) mounting, and (6) decalcifying.

The first and second have already been described (Chap. V.) It now remains to give particulars regarding the others.

STAINING REAGENTS.

I. Carmine and its Compounds.

(*a*) *Ammoniacal Solution of Carmine.*

Pure carmine	4 grm.
Strong liq. ammoniæ . . .	6 c.c.
Water	120 „

Make the carmine into a paste with a little of the water in a mortar, add the ammonia, and when thoroughly mixed, the remainder of the water.

(*b*) *Borax-Carmine* (Grenacher).

Carmine	0·5 grm.
Borax	2·0 „
Distilled water	100 c.c.

These are mixed in a porcelain evaporating dish, and heated to boiling. To this bluish-red liquid, dilute acetic acid (about 5 per cent) is added till the colour changes and comes to be more like that of ammonia carmine. It is allowed to stand for twenty-four hours, decanted, and is then filtered. A drop of carbolic acid is added for preservation purposes. Friedländer (No. 10) recommends washing the preparation in the following after it has lain for a few minutes in the borax-carmine.

Hydrochloric acid	1 c.c.
Alcohol	70 „
Distilled water	30 „

This borax-carmine stains nuclei intensely and rapidly. It should be kept in readiness for particular preparations. Experience alone will teach for which tissues it is most suitable.

(*c*) *Picro-Carmine.*—Many receipts are given for this. Ranvier's original receipt is the following:—Dissolve 1 gramme of pure carmine in 10 c.c. water and 3 c.c. liquor ammoniæ in a mortar. Add this to the 200 c.c. cold saturated solution of picric acid. Evaporate, either on a water-bath or by exposure to the air, down to one-third of its bulk, and filter.

This is a most serviceable double stain, and is suitable for preparations to be mounted in Farrants' solution or glycerine jelly. Certain tissues have a peculiar affinity for picric acid, such as horny epidermis and the matrix of bone, while the carmine picks out the nuclei of cells. Most beautiful pathological preparations may sometimes be obtained by the contrasts of these two effects. The fluid has to be poured on the section, left in contact with it for a couple of minutes, and the excess run off. The section must on no account be washed in water. The Farrants' solution or glycerine jelly is simply dropped on it while saturated with the stain, and a cover-glass applied. The proper reaction does not usually take place for several days after the preparation is mounted; it sometimes requires as many months.

(*d*) *Picro-lithium Carmine.*—This is even preferable to the foregoing, as it stains more rapidly, and with greater certainty. Friedländer (No. 10) gives the following receipt:—Dissolve 2½ grammes carmine in 100 c.c. saturated solution of lithium carbonate. To this add from 2 to 3 c.c. of a saturated solution of picric acid.

(*e*) *Carmine and Freezing Fluid.*—An excellent weak staining liquid for large naked-eye sections of brain, or for sections of medulla, pons, and cord, when cut in series, is the following:—

Freezing fluid "A" (Sect. 37) . .	8 parts.
Ammoniacal solution of carmine .	1 part.

The advantage of this solution rests in the fact that it does not stain too quickly, and hence in a large section its action is more equable than that of a stronger dye. It also effectually prevents segments or microscopic sections of brain from swelling irregularly, which is liable to happen when they are hardened in Müller's fluid, and transferred to a liquid of less density. A mixture of syrup alone does not suit for making this staining fluid; the gum contained in the freezing fluid seems to act in precipitating the carmine on the tissue.

(*f*) *Alum-Carmine* (Grenacher).—Dissolve 1 gramme of carmine in 100 c.c. of a 5 per cent solution of alum. Boil for about twenty minutes, and filter when cool.

(*g*) *Indigo-Carmine* (Merkel).—Flesch recommends hardening tissues which have to be stained in this by means of chromic acid or Müller's fluid, and subsequently completing the hardening process in methylated spirit. It is specially suited for nervous tissue, and for ossifying cartilage. The dye as used is a mixture of solutions of borax-carmine (carmine 2, borax 8, H_2O 130) and of indigo-carmine (indigo-carmine or sulphindigolate of soda, and borax, each 8, and water 130) in equal parts. The mixture decomposes if kept longer than a week, and the carmine stains too deeply. Textures should be left in it for twenty-four hours at ordinary temperatures, and from one to two hours when in an incubator. After staining, the superfluous colour is extracted by means of a saturated solution of oxalic acid. Preparations may be mounted in Farrants' solution or balsam.

II. **Hæmatoxylene.**—The following solution will be found excellent for ordinary staining of nuclei.

(*a*) *Nucleus Staining Hæmatoxylene.*

Hæmatoxylene	12 grm.
Alum	50 „
Glycerine	65 c.c.
Distilled Water	130 „

Boil, and while hot add 5 c.c. of liquid carbolic acid. Allow the mixture to stand in the sunlight for at least a month; the longer it remains exposed the better. In course of time it assumes a deep port-wine colour, and stains nuclei of a most beautiful blue almost instantaneously after application. The solution does not decompose, nor do fungi grow upon it. If the above solution be found too strong, two expedients may be adopted. Either it may be diluted with equal parts of glycerine and distilled water; or what is better, it may be used to over-stain the section, the excess being subsequently washed out with glacial acetic acid. The preparation should be immersed in the acid until the colour changes to red. It is then to be laved in two successive vessels of water until all the acid is removed. It is sometimes advantageous to render the second water slightly alkaline with carbonate of lithia.

There is perhaps no nuclear staining reagent which is so satisfactory in its results as logwood, and when combined with some contrast stain such as eosin, Bismarck brown, chrysoidin, or picric acid, most beautiful and instructive effects can be obtained.

The tissues which stain best in it are those hardened in alcohol, and particularly if they have been actively growing (sarcomatous tumours, epitheliomata, etc.) If the tissue has been hardened in Müller's fluid, it also stains excellently, but if left for any length of time in pure watery solution of chromic acid there is the greatest difficulty in getting it to take effect.

Staining fluids made directly from logwood chips are sometimes

recommended. As, however, it is the hæmatoxylene alone of the logwood which is required, there cannot be any advantage in employing the crude material. The fluid is liable to be contaminated by tannin and other unnecessary ingredients, which materially interfere with the production of the pure colour that it ought to possess.

(*h*) *Weigert's Hæmatoxylene Stain for the Central Nervous System* (see No. 11, ii. p. 190; and iii. pp. 236-239).—This is a method devised by Weigert for the purpose of staining medullated nerve fibres in the brain and spinal cord. It is not so well suited for peripheral nerves. The stain has a special affinity for the medullary sheaths of nerve fibres, and while it colours these of a deep blue or purple, leaves the nerve-cells, axis cylinders, and neuroglia unstained. The advantages of such a reagent will be obvious to all who are engaged in studying the histology of the nervous system. The stain appears to depend upon the hæmatoxylene entering into combination with copper and being precipitated in presence of a chrome salt upon the medullary sheath of the nerve-fibre.

Weigert formerly recommended "acid-fuchsin" for the same purpose, but the logwood process is very much superior. The method is somewhat complicated, but it is to be recommended to all those working on the central nervous system. The revelations it brings out are of the most startling character, and already have gone far to modify current views on nerve physiology and pathology.

Two methods may be followed according to Weigert, the older of the two being the first described in the sequel; and although he considers the old one inferior to the more recent, yet it seems in some respects to have advantages which the other does not possess. The author has added an adaptation of the method to cutting the tissue by freezing. The technique, especially that for the brain, is thus rendered very much easier.

Method A (Weigert).—The piece of brain or spinal cord is hardened in Ehrlitzki's fluid, which has the following composition:—[1]

Potassic bichromate	2·5 grm.
Cupric sulphate	0·5 „
Distilled water	100 c.c.

It may be hardened in the cold, but it is preferable to do so in a warm chamber heated up to a body temperature. Only from three to four days are necessary for the purpose when the warm chamber is employed, but if the tissue is hardened at an ordinary temperature, a longer time is to be allowed. The hardening is completed in absolute alcohol which should be changed twice at least.

The segments of tissue are next embedded in celloidin (Sect. 38), and sections are cut in a Schanze or Weigert microtome. When cut, they are received into alcohol. They should *not* be placed in water.

They are now stained in the following logwood solution:—

[1] See No. 352, xxiii. Nos. 15 and 18, quoted by Waldeyer. No. 49, 1877, i. p. 21.

Hæmatoxylene	1 grm.
Alcohol	10 c.c.
Water	90 c.c.
Saturated solution of lithium carbonate .	1 c.c.

and are left from two to twenty-four hours in it, according to the depth of staining required. If it be desired to show simply the general direction of the fibres in the brain, two hours will be found sufficient, but if the object is to bring out the Exner's plexus in the cortex, it is better to allow the section to remain in the solution for twenty-four hours.

They are next well washed in distilled water, and will be found to be much overstained,—indeed quite black. They must consequently be placed in a decolorising solution made of the following ingredients :—

Potassic Ferridcyanide	2½ grm.
Borax	2 ,,
Water	200 c.c.

In a few minutes the gray matter should become completely visible and remain of a light brown tint, while the white retains sufficient of the stain to give it a deep violet colour. The preparation should be left in this for two hours, and be subsequently washed in water, clarified in xylol, and eventually mounted in Canada balsam dissolved in xylol.

Method B (Weigert).—The brain or cord is hardened in Müller's fluid, and the hardening is completed in absolute alcohol. The pieces from which the sections are to be cut are next embedded in celloidin, as before, and laid in equal parts of saturated solution of *neutral* acetate of copper and water for from one to two days, being meanwhile kept at a body temperature in the warm chamber.

The pieces may have a green or a brown colour after this, but it makes no difference. They are now to be placed in alcohol of 80 per cent strength, and may be retained in this till required.

They are subsequently cut, stained, and decolorised as described in method A, and mounted in Canada balsam.

The gray matter and nerve cells have a slightly brownish tint when the process has succeeded. The nerve cells can be further stained, after decolorising, with borax-carmine.

Method C (Hamilton).—The brain is hardened as described in Chapter V. Pieces about half an inch thick are placed in methylated spirit for a day if they are to be embedded in celloidin previous to cutting. If they are not to be embedded in celloidin they should remain in the spirit for three days. If the piece of brain is likely to become disintegrated when cut, it should be embedded, but if it is an entire mass this is not necessary. Let us take first the case in which it is essential to embed it in celloidin.

After being in the methylated spirit for a day the pieces of brain are transferred to a mixture of equal parts absolute alcohol and ether, and are subsequently embedded in celloidin as in A. From the methylated spirit in which the embedding process is completed they are transferred to Ehrlitzki's fluid for forty-eight hours, so as to get rid of the spirit, and are afterwards placed in the warm chamber in the following solution :—

Cupric sulphate	0·5 grm.
Potassic bichromate	2·5 ,,
Freezing fluid "B" (Sect. 37) . . .	100 c.c.

A stopper bottle should be used to hold them, so that the liquid does not become

concentrated by evaporation, and the best temperature is 98° Fahr. They are left in the warm chamber for from two to three days.

They are then ready for cutting in the ice-freezer with a planing iron in the usual way. Even the cortex, which is the most delicate of any part of the brain, will be found to cut with perfect ease, and the celloidin makes such a beautiful embedding material that the thinnest sections can be handled with impunity. The warm chamber has the effect not only of causing the copper to penetrate, but it will be found that the freezing fluid also soaks in much more thoroughly.

The sections, as they are cut, must be received in Ehrlitzki's fluid, not in water, and after they have lain in this for a few minutes, they are transferred to methylated spirit, and are thoroughly washed in it. They should now be enclosed in a layer of collodion in the following manner, so as to prevent any destruction of the section while it is staining in the hæmatoxylene. Pour some collodion over a slide and allow the superfluity to run off. When it forms a thin film bring the section out of the methylated spirit upon it, and run off the spirit until the latter becomes sodden, not dry. Pour a second layer of collodion over the section, and when it has formed a film, cut off the collodion close up to its edges. The section, embedded in a double layer of collodion, will now be found to strip off the slide with the greatest ease, and is ready for staining in hæmatoxylene, and decolorising as before. The hæmatoxylene readily soaks through the collodion, and is afterwards just as readily decolorised by the ferridcyanide solution. If it is not necessary to embed the piece of brain in celloidin before cutting, it is simply taken out of the methylated spirit and transferred to Ehrlitzki's fluid for twenty-four hours. The subsequent treatment is the same as in the foregoing.

Regeneration of the Hæmatoxylene.—As the hæmatoxylene used in all these processes is considerable, and as it is an expensive substance, some means by which it may be regenerated is worth adopting. Flesch (No. 48, iii. 1886, pp. 50-51) recommends the following:—Add 5 to 10 c.c. baryta water to about 200 c.c. of the used solution. The mixture is shaken and allowed to stand for twenty-four hours. A stream of carbonic acid gas made from marble and hydrochloric acid is then passed through it, and after twenty-four hours it is filtered. The filtered solution is said to be as good as the original.

Weigert's Hæmatoxylene Stain for Peripheral Nerves.—With normal nerves the method succeeds well, but with morbid (sclerosed) nerves it has not been found to be so serviceable. Gelpke finds that this is due to the decolorising solution being too strong. It ought to be reduced to a fiftieth of the strength recommended by Weigert.

Pal's Method for Staining Nerve Fibres.—Dr. J. Pal of the Pathological Institute, Vienna, recommends the following procedure for staining nerve fibres (see No. 6, 1888, i. p. 510):—The cord or brain is hardened in Müller's fluid, cut by embedding in paraffin, and the sections are received in absolute alcohol. They are next placed in a ⅔ per cent aqueous solution of hæmatoxylene made by boiling, with a small proportion of alcohol added. Three or four drops of lithium carbonate solution to the 10 c.c. hæmatoxylene are mixed before using. The sections are allowed to stain in this for five to six hours, at the end of which time they are washed in water, and if they do not seem to be enough stained, a few drops of the lithium solution may be added to the water in which they are washed. The sections are next "differentiated" by placing them in a ¼ per cent solution of permanganate of potash for fifteen to twenty seconds, and afterwards for a short time in Pal's solution (oxalic acid 1 part, sulphide of potassium (K_2SO_3) 1 part, distilled water 200 parts). If black specks appear on the sections, or if white and gray are not distinctly defined, place them again in the Pal's solution. The sections are then washed in water; doubly stained [illegible] carmine, or alum carmine; dehydrated in alcohol; clarified in oil of cloves; [illegible]nted in balsam in the usual way.

The "Pal-Exner" Method for Staining Nerve Fibres.—This, as described by Redfern (No. 6, 1888, i. p. 642), is said to combine all the excellencies of Exner's original method (No. 12, lxxxiii. Ab. iii. Feb. 1881), and possesses the additional advantage of the preparations being permanent.

The fresh brain or other nerve tissue is divided into small cubes, and hardened for two days in a watery solution of perosmic acid, which must be changed at least twice. The hardened tissue is then washed in water, and dipped for about two seconds into absolute alcohol. It is next embedded in wax mass or celloidin and cut in a Rivet-Leyser or other microtome. The sections are received in glycerine; are transferred from this to water, in which they are thoroughly washed; and are subsequently placed in a ¼ per cent watery solution of potassic permanganate for fourteen to fifteen seconds in order to differentiate them. They are further decolorised in "Pal's solution" (oxalic acid and potassic sulphide of each 1 part, and distilled water 200 parts). After washing in water they may be further stained in safranine or picro-carmine. The process is completed by dehydration in absolute alcohol, clearing in creosote, and mounting in Canada balsam.

Golgi's Method for Staining the Processes of Ganglion Cells.[1]—This may as well be described along with Weigert's method for staining nerve fibres. Pieces of cerebrum or cerebellum about 1 to 1½ c.c. in size are hardened in a 2 per cent bichromate of potash solution. The strength may afterwards be increased to 3 per cent. From six to eight up to thirty days are necessary to complete the hardening, and the solution should be frequently changed. The pieces are next placed in 0·5 or 0·25 to 1 per cent solution of perchloride of mercury, in which they must be retained for eight days when the pieces are small, and for at least two months if the brain is entire. It should be renewed as often as it becomes yellow-coloured, and he states that the pieces may be kept indefinitely in it. The nerve tissue, under the influence of the mercury, becomes quite colourless, while the nerve-cells stain black. Subsequent washing of the sections in sodic sulphide solution renders them darker. The sections should be clarified and mounted in some balsamic medium; or they may be clarified in solution of ammonia.

III. **Eosin.**—(Tetra-brom-fluorescein $C_{20}H_8Br_4O_5$), is obtained by the action of bromine upon fluorescein.[2]

This makes one of the best contrast stains to logwood, when the latter is used as a nuclear staining reagent. It gives with transmitted light a beautiful pink tint which has a special affinity for white fibrous and some other tissues. All cirrhotic organs can be beautifully demonstrated with it and logwood combined. The section is first stained in the logwood, and afterwards laid in a watery solution of eosin until the requisite tint is obtained. If the preparation is to be mounted in dammar lac, the eosin should be dissolved in the spirit employed for clarification. A convenient strength is ¼ per cent dissolved in water. Preparations stained with this reagent may be mounted in a fluid con-

[1] No. 49, for 1885 (1886), p. 38.

[2] Weak solutions have a beautiful pink hue compared to the rosy dawn of day. Hence the name *eosin*, from ἠώς, dawn. It is not one of the anilines, as is often stated.

taining glycerine such as Farrants' solution; it does not dissolve out. They stain in about a minute, and care should be taken not to leave them in the solution too long.[1]

IV. **Archil** (orseille) is a colouring matter somewhat like litmus obtained chiefly from the lichen *Rocella tinctoria*. It may be occasionally employed with advantage for staining animal tissues.

V. **Aniline Dyes.**—These, from the discovery of their differential colouring properties and reactions, have come to be ranked of late years among the most important of stains for pathological tissues.

Benedict (No. 27), divides the coal-tar colouring matters into three groups, namely, *basic colouring matters*, *acid colouring matters*, and indifferent or *neutral colouring matters*, according to their properties of combining with acids or bases, or with neither. The *basic colouring matters* are always used in dyeing in the form of their salts, that is, of their compounds with mineral or organic acids. They all contain nitrogen, and it is to the presence of these nitrogen atoms that they owe their basic properties. They are all derived from the type ammonia.

The *acid colouring matters* contain hydrogen atoms which can easily be replaced by metals; in other words, they possess the property of combining with bases to form salts with the simultaneous evolution of water.

The *neutral colouring matters* are not numerous; it seems that there are very few coal-tar colours which do not possess acid or basic properties. The only example given by Benedict (*loc. cit.*), is artificial indigo obtained from propiolic acid.

Aniline ($C_6H_5NH_2$) was originally derived from the products of the dry distillation of indigo in the year 1826 by Nuverdorben, but is now almost entirely obtained for commercial purposes by the reduction of nitro-benzine with nascent hydrogen. It is a colourless oil boiling at 183°, partly soluble in water (1 in 31), and acts as a strong base, forming well crystallised salts with acids. The aniline oils of commerce are a mixture of aniline with ortho- and para-toluidine (Benedict). When mixtures of aniline and toluidine are heated together with certain oxidising agents such as arsenic, chloride of tin, mercuric chloride, etc., among the various substances formed are two compounds named rosaniline and para-rosaniline. The dye stuffs comprised under the aniline colours are derivatives of these.

Animal fibres have the property of forming stable compounds with the aniline dyes, and hence are readily stained by them. Wool and silk are easily dyed with the most of them, but vegetable fibre, such as cotton and linen, are not. In order to dye, the latter a mordant must be added, that is to say, some substance to form a compound which will adhere to the fibres. Aluminium acetates, copper acetate or sulphate, ferric acetate, and salts of tin are those in commonest use. Much more has, no doubt, yet to be done in the use of mordants in the differential dyeing of pathological tissues, micro-organisms, etc., with various reagents. Weigert's hæmatoxylene-copper process before

[1] For information consult E. Fischer, No. 14, 1875, p. 349; and J. Dresch-
76.

described, and Koch's tubercle bacillus stain are examples of what magnificent results may be obtained by their use.

Much uncertainty prevails as to the exact composition of the individual aniline dyes, and they should always be obtained from reliable sources.[1]

(*a*) *Methyl-violet* ($C_{19}H_{12}(CH_3)_5N_3.HCl$), and *Gentian-violet*.—These are very closely allied in their effects, although the substances sold by the above names are probably distinct in composition. They seem to answer equally well for staining amyloid, micro-organisms, and nuclei of cells. In the first two capacities they are perhaps most useful.

Heschl (No. 12, lxxiv., iii. Ab., Jahrg. 1876, H. 1-5, p. 270, 1877), Juergens (No. 13, lxv. p. 189), and Cornil (No. 4, 1875, p. 671), seem all about the same time to have discovered the peculiar reaction which methyl-violet elicits with the amyloid substance, and gentian violet appears to have exactly the same properties.

With the amyloid or wax-like substance they give a distinct *rose pink reaction*, the surrounding nuclei fibres, etc., being stained from a dull slate blue to a bright purple, according to the quality of the reagent. Waxy tissues to be stained with this substance, should be hardened in alcohol or used fresh. They react better when hardened, and if the full reaction is to be brought out and permanently retained, they should not be hardened in a chrome salt or in chromic acid. Their action differs from that of safranine and other substances sometimes employed for staining amyloid, in respect of the resulting stain being a distinct test for the amyloid wherever it occurs, not a mere coloration. Methyl-violet sometimes goes by the name of *violet of Paris*.

The strength to employ for all purposes is $\frac{1}{4}$ per cent solution in water. If bacteria are to be stained, follow the methods described under Practical Bacteriology (Chap. viii.); if amyloid, allow the section of the tissue to lie in the solution until it is overstained and quite opaque, and subsequently wash out with dilute glacial acetic acid until the pink colour of the amyloid is clearly distinguishable by transmitted light. Various strengths of dilute acid should be tried, beginning with about 1 to 10, and increasing the strength if this does not bring out the colour satisfactorily. It is well to allow a little excess of colour to remain over and above that which will be desired permanently as the next proceeding generally removes some of it. Wash in water and place the sections in a test glass containing equal parts water and glycerine, changing this daily as long as the colour continues to exude. Mount in Farrants' solution, and if, from the section mounted some days, the colour still dissolves out into the mounting fluid, place the whole slide in water and gently remove the cover-glass. Wash the preparation and remount. It will not dissolve out after this, and the pink colour of the amyloid will be found to be brilliant, while the blue of the surrounding parts forms a charming

[1] Messrs. Beck, 68 Cornhill, London, supply them of excellent quality.

contrast. The superfluous stain may be removed with alcohol, but the pink colour never seems to be so bright as when acetic acid is used. Nothing could be more delicate than the differentiation resulting from the two colours when acetic acid is employed.

Most of the aniline dyes are insoluble in the neutral oils and fats, but methyl-violet is an exception, and hence it will be found that fat cells stain deeply with it, the resulting colour being a deep purplish blue.

(*b*) *Methyl-green* comes into commerce as a zinc double salt ($C_{19}H_{12}(CH_3)_5 \cdot N_3 \cdot CH_3Cl \cdot HCl + ZnCl_2 + H_2O$). In the year 1880 Curschmann of Hamburg announced (No. 13, lxxix. p. 556), that it also gives a reaction with amyloid. The section is treated in the same way as in the foregoing, the wax-like substance staining of an intense violet, while the non-waxy parts colour green or bluish-green. The colours, although very distinct, are not so brilliant as those obtainable with methyl-violet.

(*c*) *Rosaniline* ($C_{20}H_{19}N_3$).—This, along with some para-rosaniline, is the chief constituent of the dye known commercially as fuchsin, while magenta is the hydro-chloride of the former. The acetate of rosaniline is also sometimes sold as a magenta. It is more soluble in water than the hydro-chloride. Fuchsin is employed in pathology chiefly for staining the tubercle and cholera-bacilli, while it also occasionally stains blood corpuscles in a most remarkable manner. The blood corpuscles in certain pathological tissues (tubercular), are particularly liable to stain differentially with it, and the hydro-chloride seems to have very much the same properties. A five per cent solution in water with a little alcohol added is amply sufficient for ordinary staining purposes.

Acid fuchsin was formerly recommended by Weigert for staining nerve fibres, but its use has been entirely superseded by that of his hæmatoxylene dye (Sect. 43).

(*d*) *Methylene blue* (probably $C_{16}H_{18}N_4SH.Cl$) occurs in commerce as a double zinc salt. It makes a very delicate contrast stain for the tubercle bacillus either in sputum or in a tissue.

(*e*) *Aniline Blue-black* (probably $C_{30}H_{25}N_5$).—Attention was drawn to the remarkable power possessed by this substance in staining nerve cells by Sankey in the year 1875 (No. 28, vol. v.). The substance has two peculiar properties, firstly, that it will stain nerve tissue properly only when it is fresh and unhardened, and, secondly, that it will not penetrate into the tissue. Sankey's method consisted in staining the surface of a piece of fresh brain tissue, drying the tissue on a slide, and getting rid of the unstained superjacent layers by planing. The stained layer left lying in contact with the slide was mounted in balsam.

Lewis improved upon this system of staining nerve cells, specially those of the cortex, in the following manner (No. 29).

Sections of sufficient thinness are cut in an ether freezing microtome. An ice freezer is not suitable, as it freezes the tissue too hard and

thus injures it. The piece of tissue should be half frozen through, and a few sections selected just at the point of junction between the frozen and unfrozen parts. These are floated into a vessel filled with water. From this they are transferred to a dilute solution of perosmic acid, which has the property of slightly hardening the brain substance without interfering with the stain. The strength to use is 2 per cent, and they are left in it only for a few minutes. From this they are retransferred on a watch-glass to water, so as to remove the superfluous perosmic acid, and are then immersed in a solution of aniline blue-black ($\frac{1}{4}$ per cent), for about two hours. By this time the nerve cells are all thoroughly stained. The section is next washed in water, brought out on a slide, and allowed to dry; when quite dry, it is mounted by placing a drop of Canada balsam on it and a cover-glass.

There is no method to be compared with this for demonstrating the nerve cells of the cerebral and cerebellar cortex. Unfortunately, however, it is not so applicable to other parts of the central nervous system.

(*f*) *Bismarck or Phenylene brown* ($C_{12}H_{13}N_5 + 2HCl$) forms a capital ground-stain for tissues previously stained in hæmatoxylene. Cancerous tumours, especially those of the breast, are particularly beautiful when coloured by these two substances. The best strength, as with most of the others, is $\frac{1}{4}$ per cent, and the section is left in it only for about a couple of minutes. The addition of a little alcohol aids its solution. Mount the tissue in Farrants' solution.

(*g*) *Vesuvin* makes another contrast stain very much like, if not identical with, Bismarck brown, and may be employed for similar purposes. It is said to be identical in composition with Bismarck brown.

(*h*) *Chrysoidin* ($C_6H_5N_2C_6H_3(NH_2)_2$) may be used as a contrast stain for tubercular sputum.

(*i*) *Iodine green* is highly lauded by Gibbes (No. 15) for double staining, as it is not so opaque as aniline blue. He recommends a 5 per cent solution in water, which is to be filtered. The section must be left in this for exactly the proper time to give it the requisite colour. If it be too deeply stained, the superfluous colour cannot be afterwards removed. "It picks out all the nuclei," and "in growing bone it colours the unabsorbed cartilage." It, moreover, does not fade if the proper commodity is procured. This of late has become somewhat difficult.

Other Aniline Dyes.—Many others may be used, such as Spiller's purple, China blue, etc. Those described, however, are the most important; and the special uses to which they are put will be described under the diseases of different organs.

Very demonstrative double or treble staining may be readily effected by their employment in combination with logwood, carmine, or some other nuclear staining reagent.

Literature on General Principles of Staining with Aniline Dyes.—**Benedict**: The Chemistry of the Coal-tar Colours, translated by Knecht, 1886. **Bersch**: Die Fabri-

cation d. Anilin-farbstoffe, Wien, 1883. **Ehrlich:** Arch. f. mik. Anat., xiii. p. 263; Charité-Annalen, 1886; Zeitschr. f. wissensch. Mikroskopie, u. f. mik. Technik, iii. 1886, p. 525. **Gierke:** Zeitschr. f. wissensch. Mikroskopie u. f. mik. Technik, ii. 1885, p. 13. **Griesbach** (Azofarbstoffe): Arch. f. mik. Anat., xxii. 1887, p. 139. **Hankin** (Aniline Dyes): Quart. J. Mic. Sc., xxvii. 1886, p. 401. **Hummel:** The dyeing of Textile Fabrics (Manuals of Technology, ed. by Ayrton and Wormell), London, 1885. **Jaquemin:** Comptes rend., lxxviii. 1874, p. 1306. **Schultz:** Chemie d. Steinkohlentheers, etc. 1882. **Reeves** (How to Fix Aniline Dyes): Brit. Med. J., 1883, i. p. 450.

VI. **Nitrate of Silver.**—In staining endothelia of serous membranes, of blood-vessels, or of lymphatics, or in elucidating the structure of the cornea, there is no reagent to be compared to silver. It possesses this disadvantage, however, that it will stain the tissue only when it is living or immediately after the animal has been killed. It is consequently only in experimental pathology that it is of any use, or in the staining of recently excised parts such as tumours, etc. For the experimental study of inflammation it is quite indispensable. It has the property of staining the cement substance between endothelial cells, and hence blackens their outlines. In artificial keratitis it demarcates the inflamed from the sound parts very graphically, by showing the broken up endothelium of the plasma canals. In peritonitis it shows the germinating cells derived from the endothelium and the leucocytes exuding from the blood-vessels. The best strength is from $\frac{1}{4}$ to $\frac{1}{2}$ per cent solution in distilled water. This is to be dropped on to the part until it becomes milky, the excess washed off with care in distilled water, and the preparation, immersed in a mixture of equal parts glycerine and distilled water, allowed to become brown in the light but not in the direct rays of the sun. Care should be taken not to overstain the tissue, as all silver preparations tend to become too black by keeping. The cornea should not be placed in glycerine and water but in dilute acetic acid. After twenty-four hours, it will be found to have swollen to twice or three times its natural size, and can then be easily split into lamellæ. The endothelium of lymphatic vessels in a transparent tissue, such as the central tendon of the diaphragm in the rabbit and guinea-pig, can be readily stained by dropping on a $\frac{1}{4}$ to $\frac{1}{2}$ per cent solution, and subsequently washing in distilled water.

VII. **Terchloride of Gold.**—This is open to the same objection as silver, namely, that in order to be satisfactory the staining must be done in a perfectly fresh tissue. A great deal of uncertainty is attached to this method of staining, chiefly due to the different qualities of gold chloride which are to be purchased. There seems to be an impurity in some of them which invalidates their power of staining. The pathological tissues for which it should be employed are the artificially-inflamed cornea, tendon, or cartilage, or, in fact, any inflamed connective tissues. It is not to be recommended for the central nervous system as its action is so uncertain, and as all its best effects can be brought out by Weigert's hæmatoxylene stain (Sect. 43).

A pretty strong solution is usually best, about 2 per cent being most serviceable where the tissue is dense, but it may be diluted for other tissues down to ½ per cent. The usual procedure is to soak the tissue in the solution for half an hour or less, to wash in distilled water, and to expose to daylight in water slightly acidulated with acetic acid until a purple colour results.

Ranvier's well-known method (No. 18) consists in soaking the fresh tissue in lemon juice for from five to seven minutes. It is next washed in distilled water, and left in the gold solution for twenty minutes to half an hour. It is again washed in water in order to get rid of the superfluous gold, and allowed to stain in the dark in a mixture of 1 to 4 formic acid and water. The gold is usually completely precipitated upon the preparation in twenty-four hours, if the staining is going to succeed.

This method is not so useful as the former for connective tissues, as the formic acid is liable to destroy endothelium; it is recommended mainly for tracing the course of nerve fibres.

VIII. **Perosmic Acid.**—No pathologist ought to be without this reagent. It is convenient to keep it in a stopper bottle as a 1 per cent solution in distilled water. All organic matter should be removed from the bottle previously by rinsing it with sulphuric acid and subsequent washing, and light should be carefully excluded. A ½ per cent solution is the usual strength to be employed for pathological tissues. It blackens all fatty and caseous degenerations or infiltrations; and as it brings these prominently into view is naturally a valuable test for them. It, further, stains ordinary tissues of the most delicate gray-brown or gray-green tint, and sharpens the outlines of cells and fibres.

The usual instructions given for its use as a staining reagent are to put the fresh unhardened tissue in a ⅙ to ¼ per cent solution in water. A far more delicate stain is, however, obtained if the tissue be first hardened in Müller's fluid, cut, and *the section* then stained in a ¼ to ½ per cent solution. Two methods of staining can be adopted, the latter of which is specially useful for pathological tissues. The first is to lay the section in the solution for twenty-four hours, to wash it in distilled water, and to transfer it to preservative fluid (Sect. 40). The second is simpler, but requires longer time. Add a little of the solution, about 1 part in 10, to the preservative fluid, mix them, and leave the section in this mixture until it is sufficiently blackened.

It makes an excellent combination stain with picro-carmine, some of the effects in flat-celled epitheliomata, cirrhotic kidneys, and liver being most charming. The tissue is first stained in perosmic acid by either of the above procedures; it is next thoroughly washed; and is subsequently stained in picro-carmine.

All tissues stained in perosmic acid, or in this combined with picro-carmine, ought to be mounted in Farrants' solution or glycerine jelly.

As a hardening reagent it may also be employed for certain tissues, but is not nearly so serviceable in this capacity as in that of a stain.

IX. **Iodine staining fluid** is used for organs affected with the wax-like disease. It should be made with Liquor Iodi (Phar. Brit.) and water, of such strength as to assume a light brown colour. It ought

to be kept in a stopper-bottle, and when used the section is placed in a test-glass half filled with the solution and moved about with a needle so as to bring it in contact with as much of the iodine as possible. It ought not to be too strong for microscopic purposes, not nearly so strong as that previously recommended for naked-eye staining. Immediately on the amyloid part of the section assuming a brown colour, it should be removed, placed in a basin of water, and rapidly mounted in iodine mounting fluid (Sect. 45). The stain is so volatile that a great part of it will be lost if exposed too long. Tissues to be stained with iodine should either be fresh, or, what is better, hardened in alcohol. Those hardened in chromic acid or its salts never give the reaction satisfactorily, nor is it permanent in them. Sections of wax-like organs stained with iodine should be employed only for low powers of the microscope (50 diams.); methyl-violet is infinitely more delicate and precise as a staining agent. The cover-glass should be cemented as soon as possible so as to prevent the iodine escaping.

If looked at with transmitted light the waxy parts have the colour of red mahogany, and the reaction is not at all distinctly seen. In order to bring out the true mahogany brown colour, the preparation must be examined with direct light.[1] The waxy parts will then be easily distinguished from the surrounding tissue. Remember that the whole section stains with iodine; but the waxy part stains dark brown, while the parts which are not waxy stain iodine yellow.

Literature on General Methods of Staining.—**Arnstein** (Methylene Blue): Anat. Anz., ii. 1887, p. 551. **Babes** (Safranin): Arch. f. mik. Anat., xxii. 1883, p. 356. **Cheyne**: Practitioner, xxx. 1883, p. 241. **Dekhuysen**: Centralbl. f. d. med. Wissensch., xxiv. 1886, pp. 931-945. **Ehrlich** (Methylene-Blue Reaction of Nerve Tissues): Deut. med. Wochnschr., xii. 1886, p. 49. **Lustgarten** (Victoria Blue for Nuclei and Elastic Fibres): Med. Jahrb., 1886, i. p. 285. **Pfeffer**: Zeitschr. f. wissensch. Mikroskopie u. f. mik. Technik, iii. 1886, p. 542. **Sahli** (Double Staining of Nervous System): Ztschr. f. wissensch. mikr., ii. 1885, p. 13. **Schiefferdecker** (Weigert's Hæmatoxylene for other Nerve Elements): Anat. Anz., ii. 1887, p. 680. **Schultze** (Vital Methylene-Blue Reaction of the Cell Granule): Anat. Anz., ii. 1887, p. 684. **Seguin** (Staining Large Sections of Brain): Med. Rec. N. Y., xxvii. 1885, p. 184. **Stirling** (Double and Treble Staining): J. Anat. and Physiol., xv. 1880-1, p. 349; *also* (The Sulphocyanides of Ammonium and Potassium): J. Anat. and Physiol., xvii. 1882, p. 207. **Renant** (Eosin and Glycerine Hæmatoxylene): Arch. de Physiol. norm. et path., viii. 1881, p. 640. **Unna** (Chemical Theory): Arch. f. mik. Anat., xxx. 1887, p. 38.

Clarifying Reagents.

44. With preparations which are mounted in Farrants' solution or glycerine jelly, no further clarification is necessary than that which is produced by these media. Where Canada balsam or gum dammar is to be employed, some means of clarifying the preparation before mounting is requisite.

[1] On a bright day it is sufficient simply to turn round the dark side of the mirror; but if the light be insufficient, a condenser must be resorted to.

The section, immediately after being cut, ought to be floated in a basin of water until all the air-bells have disappeared, and until the freezing fluid is removed. It is then placed in a second basin of water and transferred to a slide. In doing so the slide is held perpendicularly in the left hand and should be immersed about three-fourths in the water. Do not lay it horizontally under the section, and endeavour to withdraw the latter upon it in the horizontal position, as almost to a certainty it will be carried off the slide by the excess of water. With a *needle* drag one edge of the preparation on to the dry upper part of the slide. It will stick to it, and the slide may now be withdrawn. Very probably the section will be folded at the upper edge. The folds are unravelled by reversing the position of the slide so as to immerse the folded part in the water, and by shaking gently. Never on any account touch the preparation with camel's-hair brushes. There is no means by which a delicate section of perhaps an inch to an inch and a half in diameter can be spread out without injury, unless by floating it in some liquid.

The slide is next to be dried by placing it upright for a few minutes and subsequently removing the water with a piece of old linen rag, or, what is often as good, with the finger. When as much of the water is got rid of as possible without actually drying the preparation, methylated spirit is allowed to run over it, the excess being drained off at one end of the slide. Three applications of the methylated spirit are usually enough. The preparation, however, must be moved, so as to ensure that the spirit gets completely underneath it. Absolute alcohol is next allowed to run over it and to soak thoroughly into it in a similar fashion, one application of this being sufficient. It is now ready for the clarifying reagent.

The chief clarifying media which are employed are oil of cloves, turpentine, creosote, xylol, and oil of bergamot. There are several other essential oils which may also be used. In selecting a particular clarifying reagent, the following ought to be the guiding principles:—Oil of cloves is perhaps the most powerful and the most convenient, as it does not readily evaporate, and so can be left exposed without danger of the section drying. Where a preparation, however, is stained with an aniline dye it should be avoided, as in course of time it destroys the stain. Xylol is much the best for such; and if a solution of Canada balsam or gum dammar is to be the mounting medium, these should be dissolved in xylol. Weigert's hæmatoxylene stain for nerve fibres also fades when oil of cloves is employed, and hence xylol is likewise preferable for sections so stained.

The spirit is to be allowed to evaporate until the section assumes a sodden appearance, but on no account must it be allowed to dry. If it dries, it will be spoilt. What should be aimed at is merely to remove as much *superfluous* spirit as possible before the clarifying agent is applied. With a goat-hair or sable-hair brush, slip a drop of the clarifying fluid *under* one corner of the preparation, and hold the slide at such an inclination that the drop will readily find its way *under* the whole section. This can easily be accomplished, even in the largest sections, if too much spirit is not allowed to evaporate. The great point to be attended to is to insinuate the drop of clarifying fluid *under* the preparation, so that the heavy oil of cloves or bergamot, as the case may be, will the more readily displace the lighter spirit. If

this is successfully accomplished, without allowing any of the oil to run over the surface, the section will clarify almost instantaneously. Should any part of the preparation remain milky, too much spirit has been left upon it, or the alcohol finally applied has not been absolute. To hasten the clarification in such a case, place the slide for a few minutes on a warm surface, such as a mantelpiece.

When the clarifying agent has found its way through the section, and the spirit has flown off, the surface of the preparation should be touched all over with the clarifying agent by means of the brush. The superfluity is allowed to run off, the slide is dried close into the edge of the section, and is mounted in Canada balsam or gum dammar.

The method of clarifying and mounting is suitable for several tissues, but should by no means be universally adopted. With most pathological objects, it gives an entirely artificial and erroneous impression of their structure. It is well suited for injected preparations, for the central nervous system, and for demonstrating several other pathological conditions to be afterwards described in detail. It should, however, never be employed alone; an unclarified preparation mounted in Farrants' solution should always be examined collaterally with it.

A copper "lifter" is sometimes recommended for transferring the preparation to the oil of cloves. This is unnecessary, as the whole operation of clarifying can be conducted on the slide much more quickly and with less chance of injury to the section.

Where embryos or other small objects are to be embedded in paraffin, it is better to clarify the whole embryo before cutting it, as the paraffin adheres much better than when the embryo is simply placed in it out of spirit. So long as the object is small this can be readily done by placing a little oil of cloves in the bottom of a porcelain dish or watch glass and immersing the embryo or other body, previously soaked in absolute alcohol, in it for twenty-four hours or longer.

Where an essential oil is inadmissible for the clarifying of a section, creosote may be substituted. It renders sections of brain and spinal cord very transparent in a short time. It should be used in the same way as oil of cloves.

Mounting Fluids.

45. The choice of a mounting fluid depends upon the nature of the tissue, its staining, and whether it has been clarified or not. They may be divided into two sets according as the tissue can be mounted in the medium directly from water, or requires first to pass through spirit and a clarifying reagent. Among the former are to be included Farrants' solution, camphor mounting fluid, iodine mounting fluid, glycerine jelly, and glycerine; while the most important in the latter are the various solutions of Canada balsam and gum dammar in chloroform, turpentine, benzole, xylol, etc. The two sets are distinguished by the letters A and B.

Set A. (Sections mounted in these do not require to be clarified).

(1) *Farrants' Solution.*—Of all mounting fluids for pathological tissues this is by far the most convenient and trustworthy. It is trustworthy, because one is certain that it will not give rise to an artificial appearance from over-clarification, as is often the case when solutions of Canada balsam or gum dammar are employed. It seems to be a perfect preservative when properly made, the appearance of the tissue often improving the longer the preparation is kept.

The original receipt, as given by Farrants, was to make a mixture of equal parts of glycerine, saturated solution of arsenious acid, and mucilage of gum acacia. This will be found, however, to contain too little gum, and the following modification will be found better (Hamilton):—Make a saturated solution of arsenious acid in distilled water by boiling. Allow it to stand for twenty-four hours and filter. Mix equal quantities of this, glycerine, and water, and add sufficient picked gum acacia to convert the liquid into a thick syrupy fluid. It is best to allow an excess of gum to stand for a week or so in the solution, stirring daily, and then to drain off the liquor from the residue. It must now be slowly filtered through paper, the paper being changed every day.

This medium should not be employed for a preparation stained in silver, gold, or iodine, nor for one which has been injected with Prussian blue; but, with these exceptions, there is hardly a pathological tissue for which it is not available. It is earnestly to be desired that a medium possessing a refractive power not higher than this be employed more frequently than such mounting fluids as Canada balsam or gum dammar. This ought to be remembered when the object is intended for high powers of the microscope even more than when the magnifying power is to be comparatively low. Each set of media has its advantages, but for the generality of tissues the transparency obtained by those classified under "A" is much to be preferred to the somewhat artificial effects brought out by those included under "B."

It should always be kept in mind, however, that as Farrants' solution does not render the tissue much more transparent than it is naturally, extremely thin sections must alone be mounted in it—a proceeding which is infinitely superior to that of making a thick section diaphanous by an artificial clarifying reagent.

If it is desired to make a preparation mounted in Farrants' solution very transparent, it should be placed without being cemented in a warm chamber (100° Fahr.) with free ventilation, for several days. The longer it is left, the more transparent it will become, until a transparency almost equal to that of oil of cloves may be obtained. It must be cemented with zinc white as soon as it is removed from the warm chamber. This is often useful where it may be inconvenient to mount the preparation in balsam, or where a degree of transparency, intermediate between that obtainable by this substance and Farrants' solution, may be desired. Very demonstrative *naked-eye* preparations of the medulla and pons may be made in this way.

The section to be mounted in it should be taken out of water in the same manner as that formerly recommended. All the water should be removed from the slide close up to the preparation, and as much as possible from the preparation itself without drying it. A drop of the medium is now allowed to fall upon it, care being taken not to churn up air-bells in the bottle by drawing the glass rod out too quickly. It is next covered with the cover slip, pressed gently down, the superfluous medium removed with a soft rag, and left in a dry place for ten days to a fortnight before being cemented.

(2) *Camphor Mounting Fluid* (Hamilton).—In order to avoid the decomposing action of the arsenious acid upon various metallic stains a mixture made virtually on the same principle as Farrants' solution, but containing camphor instead of arsenic, may be substituted. The receipt is the following :—

Camphor water	2 parts.
Glycerine	1 part.

Saturate with picked gum acacia as in making Farrants' solution, and filter through paper. Keep in a stopper bottle with several small pieces of camphor floating in it.

It is chiefly useful for Prussian blue injections.

(3) *Iodine Mounting Fluid* (Hamilton).—This is employed for mounting sections of waxy organs stained in iodine. The section is stained in the manner described under staining fluids, and a large drop of the fluid is placed over it. A cover-glass is adjusted, but should not be pressed down. It, like the camphor medium, is made essentially in the same way as Farrants' solution, but iodine is added instead of arsenic or camphor.

Take of Glycerine	1 oz.
„ Water	2 „
„ Liquor iodi (Phar. Brit.) . . .	½ „

Saturate with picked gum acacia as before and filter through paper. Keep in a stopper bottle.

(4) *Glycerine Jelly* (Hamilton).—To make a good glycerine jelly for microscopic purposes, there should be as little water in its composition as is consistent with the melting and subsequent consolidation of the gelatine. What one desires in this medium is as much glycerine as possible with just sufficient gelatine to cause it to gelatinise.

A quantity of French gelatine is soaked in water until it becomes pliable (about ten minutes). The water is roughly run off from it, or it may be partially dried in a towel. It is next melted, and 15 ounces of this and 30 ounces of glycerine are measured out. The white of an egg is beat up with half of the glycerine, while 1 ounce of liquid carbolic acid is added to the other half. The gelatine is allowed to cool as much as possible, without actually causing gelatinisation. The glycerine containing the white of egg is then added,

and the two are boiled within a flask in a water bath. When the egg begins to precipitate in flakes, the other half of the glycerine, containing the carbolic acid, is to be added and the whole mass boiled until it separates into a clear liquid and a tough albuminous scum. It is now passed through muslin to remove the albumin, and subsequently filtered through paper. The latter is a somewhat tedious operation, and a hot water filter should be employed, or the filtering apparatus may be set down at a short distance from a fire, the paper being frequently changed. The resulting liquid will be found to be quite transparent, and to be a perfect preservative.

When about to be used, it should be melted in hot water and dropped on to the section, a cover-glass being immediately applied and gently pressed down. It gelatinises in a few minutes. The superfluous jelly is cut off, and the cover-glass secured with a ring of white zinc cement.

This forms a beautiful mounting medium, and can be adapted for all purposes to which glycerine or Farrants' solution is applicable. It should not be exposed to the atmosphere, as it rapidly absorbs water.

(5) *Glycerine*, although it makes when in combination one of the most serviceable of mounting fluids, is not to be recommended by itself, unless perhaps for tissues stained in silver or gold, and, even with these, glycerine jelly will be found to be preferable. It is disadvantageous, firstly, because it is very difficult to cement the preparation so as to prevent it from oozing out; and, secondly, because it is not a perfect preservative. The foregoing mixtures, into whose composition it largely enters, are preferable.

Set B. (Sections mounted in these all require to be previously clarified.)

(1) *Canada Balsam.*—This may be used in its pure state for mounting micro-organisms dried on a slide, or for bone. With other more delicate structures it is too thick and requires to be dissolved artificially.

(2) *Canada Balsam and Xylol.*—Place some Canada balsam in a wide-mouthed stopper bottle in a warm chamber or by the side of a fire, the stopper being withdrawn. Allow it to remain until, when cold, it forms into a hard cake.

Add one and a half times its bulk of xylol, and replace the stopper. Stir the mixture daily until the balsam is dissolved. Filter through paper, and if it gets too thick in filtering, add a little more xylol and renew the filtering paper.

Where a section is stained with an aniline dye or with Weigert's hæmatoxylene, this medium is to be preferred to the following, as it does not cause the stain to fade. Preparations to be mounted in it should have been previously clarified in xylol or oil of bergamot. Oil of cloves may be employed in the first instance, as it clarifies so readily, and be subsequently washed off with either of the above.

(3) *Dammar Lac.*—Klein (No. 16) gives the following excellent receipt:—

Gum dammar	½ oz.
Gum mastic	½ ,,
Turpentine	1½ to 2 fl. oz.
Chloroform	2 ,,

The gum dammar is dissolved in the turpentine, and the mastic in the chloroform. The two solutions are filtered separately and subsequently mixed.

The above solid constituents may also be dissolved in 4 ounces of benzole and filtered. This solution dries quicker than the other, and perhaps is not so liable to cause stains to fade.

In making either of these the greatest care should be taken that the vessels employed are perfectly dry. It is well to rinse them out first with alcohol and subsequently with chloroform or turpentine before using.

Both solutions are best suited for preparations clarified in oil of cloves.

Covering the Preparation and Cementing It.

46. Care should be taken that the cover-glass is very thin, as it is disappointing to find after finishing the preparation that it cannot be examined with a high power of the microscope, or with an immersion lens on account of the thickness of the glass. A drop of the mounting fluid is put on the section, and the cover-glass, sustained between the forefinger and thumb of the left hand at an angle of about 45°, is approximated to the drop until the lower edge touches it. A needle is held in the right hand, not as a writing pen is, but parallel to the table, as one in fact holds a violin bow. It is slipped under the upper edge of the cover-glass, and the latter is gradually lowered over the drop of mounting liquid.

The best cement for all preparations is made of the following constituents:—

Gum dammar	2 oz.
White oxide of zinc (finely ground) . .	2 drs.
Benzole	2 fl. oz.

Dissolve the gum dammar in the benzole, and mix the zinc with it in a mortar. Filter through muslin.

Farrants' solution or glycerine jelly preparations may be directly surrounded with this; but if the preparation be mounted in solution of Canada balsam or gum dammar, it is necessary first to put on a ring of liquid glue to prevent the cement from running under the cover.

The ring should be made on a turning table and a goat's-hair brush. In cleaning a Farrants' solution preparation previous to cement-

ing it, the following method is to be adopted :—The cementing should not be done until the preparation has been mounted for ten days to a fortnight; and during this time the slide should have lain in a dry place, so that the mounting fluid becomes hardened at the edge. The hardening is greatly accelerated by placing it in a warm chamber, but the preparation may thus be made too transparent if not carefully watched. The slide is held in a basin of water, and with a few touches of a large camel's-hair brush all the superfluous Farrants' solution can be removed. The cover-glass will not be detached, if it is done quickly, as the medium has become sufficiently hard at the edge to fix it. The slide is next rapidly passed through clean distilled water, and placed in a gently-sloping position to dry. When dry, the cover-glass is encircled with a ring of white zinc cement.

Decalcifying Fluid.

47. For the purpose of depriving a tissue of its earthy salts the mixture formerly recommended (Sect. 36) should be employed. Care must be taken that it is frequently changed. The bone or other calcic part, after being subjected to its action, becomes quite pliable.

CHAPTER VII

THE MICROSCOPE

48. It is not intended to give a detailed account of the optical principles of the microscope. Such would be quite apart from the scope of this work; and as the subject has been treated so exhaustively elsewhere, it will be advisable for the reader, wishing to get a thorough insight into the matter, to consult such treatises as those contained in Dr. Carpenter's work on the microscope, Professor Rutherford's *Outlines of Practical Histology*, *Das Mikroskop* by Dr. L. v. Thanhoffer, or *Das Mikroskop* by Dr. Leopold Dippel. The few remarks which follow will be devoted to guiding the reader in procuring a serviceable instrument.

The compound microscope of the present day consists of a long brass tube or two short tubes, the one telescoped into the other, with a combination of plano-convex lenses known as the *objective* at the lower end and the *eye-piece* at the upper. Along with this there are a mirror and other mechanical arrangements for condensing and modifying the light brought to bear upon the objective. The objectives of most makers consist of three compound plano-convex lenses of crown and flint glass, while the eye-piece, if it be that of Huyghens, the one in common use, is composed of two plano-convex lenses, the lower being known as the field glass.

49. **Illumination of the Microscope.**—The pathologist should work as little as possible with artificial light. It is useless for naked-eye objects, and it is bad for the examination of those which are microscopic. For microscopic purposes a clear day and a northern exposure are to be desired. The direct rays of the sun should, of course, never be employed. If it is absolutely necessary to work by night a very good light is obtained from an ordinary gas or lamp light, if a piece of obscure glass is interposed between the light and the microscope. The light ought to be taken from a *flat* surface, not from a convex surface such as that of an ordinary globe.

A Mirror is placed below the stage, and is for the purpose of

throwing the light upwards through the object to be viewed. It may have a double or a single surface. When single it is usually slightly concave, when double one side is concave, the other flat. The concave surface is for ordinary illumination with transmitted light, while that which is flat is to be employed along with an achromatic condenser.

The Diaphragm.—There are usually three kinds of diaphragm met with on microscopes by various makers. The commonest is simply a plate of blackened metal with variously sized round apertures punched out in it, which turns on a pivot beneath the stage. Another form, which is not nearly so convenient to work with, consists of a series of brass cylinders with different sized apertures in them, which are made to fit into a tube inserted in the stage. They have the advantage of admitting the light as close to the object as possible. The third is the most ingenious "Iris" diaphragm, invented by Brown (No. 17, vol. xv. p. 74), by which an aperture of any required size can be obtained by simply moving a lever.

The proper use of the diaphragm is apt to be disregarded by beginners, and this is sure to cause the object to be indistinctly defined. One of the first things to attend to in focussing an object is the regulation of the light admitted. Those who are not accustomed to use the microscope generally fail to illuminate the object properly from two causes, firstly, because the light is not properly centred upon the objective; and, secondly, because the aperture in the diaphragm selected is not of the right size. For low powers a large aperture may be employed, but for high powers and with a dry lens one of medium size is to be chosen. Trial alone will demonstrate what objects are best seen with a small amount of light, what with a large.

Direct and Oblique Illumination.—For pathological objects the light is usually transmitted from the mirror in the optic axis of the microscope. In examining certain objects, such as diatoms, it is often advantageous, in order to show the fine markings upon them, to transmit the light more or less obliquely. This obliquity, when of small angle, may be obtained by simply shifting the position of the mirror, or by stopping out the central rays derived from an achromatic condenser. When a greater degree of obliquity is required special instruments, such as Amici's prism or a parabolic illuminator, are used for the purpose. The light may be oblique, and yet be able to penetrate the entire system of lenses in the objective, or it may be so oblique that the light transmitted through the microscope is only that secondarily reflected from the object itself.

The method of oblique illumination, however, possesses little if any practical value in ordinary histological work, useful as it may be in examining diatoms and such like objects.

A Substage Condenser is necessary when working with high powers, and the optical combination known as **Abbe's Condenser** is usually employed for bacteriological work. The author prefers that of Zeiss's

own manufacture to the imitations of it by opticians in this country. The high-angled achromatic condensers of English make (Powell and Lealand, Beck, and Swift) are, however, equally as effective both for bacteriological and histological purposes, if not preferable in some respects for the latter, and the student whose microscope is fitted with one of these can well dispense with an Abbe.

50. **Angle of Aperture.**—Lenses are made of wide or of narrow angle of aperture. By the angle of aperture of a simple lens is meant the angle formed between its borders and a luminous point placed in focus. In the compound system, however, of a microscopic *objective*, many of the peripheral rays do not pass through the entire system of lenses; and hence the angle of aperture in such is understood to be *the angle formed between a luminous point placed in focus and the most peripheral rays which are capable of passing through the entire system.* It is thus quite different from the angle formed by the margin of the *lowest lens*, and a luminous point when in focus. Hence the size of the *actual* aperture or diameter of the lowest lens is no indication of the size of the angle of aperture, so much so that its margin may sometimes be accidentally chipped without impairing the usefulness of the microscope. The less the focal distance, the larger the angle *ceteris paribus* will be.

The larger the angle the greater the amount of light passing through the lens, and with very high powers this, of course, is a great desideratum. But it will be found that lenses of wide angle (130° upwards), lose in penetrating power, that is to say, the strata alone which are exactly in focus will be sharply defined, while those immediately above and below will be only dimly perceptible.

Seeing that a wide angle objective admits rays of greater obliquity than one of narrow angle, the former will have more "resolving power," as it is called, than the latter, that is to say it will define minute markings upon diatomaceæ and such-like test objects better than the latter will, and hence may seem to be the finer lens. The inferiority of the wide-angled lens, however, for histological purposes becomes manifest when an actual histological object is examined, and hence in choosing a lens for pathological work the usual test objects supplied by the makers such as *Pleurosigma angulatum* or *Podura scales* should not be alone employed. The same kind of effect is brought out with a wide angle lens, as with one of low angle when the illumination is oblique. The cause of the wide-angle lens having such good resolving power but feeble power of penetration depends upon the fact, that the latter decreases inversely with the square of the former.

For lenses giving with a medium power eye-piece an amplification of 250-300 diameters (*e.g.* $\frac{1}{4}$ or $\frac{1}{6}$ inch), and intended especially for histological work, a certain degree of penetration is indispensable, and the student, therefore, in choosing such a lens as his "high power" for ordinary work, should certainly give preference to one of medium angle (80°-100°).

51. **Dry and Immersion Lenses.**—Objectives are of two kinds, either *dry*, in which air alone intervenes between the lowest lens and the cover-glass, or *immersion*, as they are called, in which a drop of some liquid having a greater index of refraction than air, fills up the interspace. Of the liquids employed, water and certain other still more refractile substances, such as cedar-wood oil, a mixture of fennel and ricinus oils, or a mixture of chloral hydrate or iodide of zinc and glycerine, are the chief. Those in which essential oils or solutions of salts are used are known also as homogeneous immersion lenses, because these substances have very much the same refractile index as the crown glass of which the front lens of the objective and the cover are composed, the combination thus constituting a homogeneous whole. Two objects are gained by substituting oil or water in place of air between the objective and the cover-glass. In the first place, on account of the greater refractile index of the substances employed as compared with air, more rays are bent inwards and enter the lens, and hence more light is gained; and, in the second, the angle of aperture of the lens is thereby increased, and, consequently, the "resolving power" of the instrument augmented.

The oil or water is placed in a drop on the centre of the cover, and the lens is brought down until it touches it. The object is then focussed in the usual way. Oil immersions are now used for all delicate definition of high-power objects, such as that of micro-organisms, and are decidedly preferable to water immersions. The lens should be very carefully cleaned with a piece of old washed linen rag after use, and care should be taken that the oil does not touch the cement of the cover-glass as it is apt to dissolve it. Oil immersions have the great advantage of not requiring a correction collar for cover-glasses of different thickness, unless in the very finest work; and, as a rule, those of the best makers are unprovided with anything of the kind, and are perfectly serviceable for all pathological details. The correction collar, which is usually appended to high power dry and water immersion lenses, acts by separating or approaching the system of lenses composing the objective according to the greater or less thickness of the cover-glass, and there is often considerable difficulty in hitting the exact point at which the lens shows best.

52. **Abbe's Apochromatic Lenses.**[1]—The chief efforts of opticians up till lately have been expended in endeavouring to increase the *numerical aperture*[2] of objectives. It is questionable, however, when this goes beyond 1·3 or 1·4 whether much can be gained. Abbe long ago recognised this fact, and of late turned his attention rather to

[1] The author is indebted for much of the information contained under this title to the translation by Mr. Miers of Professor Abbe's paper and to Mr. Aldolf Schulze's excellent paper on the subject (see Bibliography).

[2] Abbe defines the *numerical aperture* as the product of the sine of the semi-aperture of a micro-objective and the refractive index of the medium in which its front lens is immersed.

the improvement of the **definition**, that is to say, of the better correction of **spherical and chromatic aberrations**.

With the crown and flint glass in common use for the manufacture of microscopic objectives, much advance in this direction was hardly possible; and, accordingly, he instituted an inquiry at the hands of Dr. O. Schott of Witten in Westphalia, as to whether other kinds of glass could not be composed possessing the necessary properties. Out of more than a thousand different glasses compounded and examined by the spectroscope refractometer, he was able to select a few which had the necessary properties. The new glasses contain, some of them, as many as fourteen elements, but the chief constituents appear to be silicates, borates, and phosphates.

The objects aimed at were to obtain crown and flint glasses in which the dispersion for the different regions of the spectrum should approximately possess the same ratio, and thus get rid of the so-called "secondary spectrum"; and to increase the number of optical media in such a way that, with the same refractive index, the dispersion, or, with the same dispersion, a refractive index, might be obtained, not, as hithero, merely in combination with flint glass of high dispersive powers, but also with lower dispersion, as in crown glass.[1]

Advantages gained.—(1) One of the main results achieved by these new lenses has been to render it possible to bring three colours to one focus, whereas in the older lenses it was not possible to correct the spherical aberration for more than one. They have been called *apochromatic* lenses on account of their superior powers of correcting spherical and chromatic aberrations.

(2) The full value of the large apertures becomes apparent owing to their superior corrections.

(3) They will stand a much higher eye-piece (one giving an amplification of 12 to 15 diams.)

(4) They are excellently adapted for micro-photography from the correction being so perfect that the visual and actinic foci coincide.

(5) The increased spherical and achromatic corrections give a much larger concentration of light.

(6) The objects viewed by them appear in their natural colours.

Compensating Oculars. Zeiss has constructed suitable oculars under the above name. They are designed to overcome the residue of peripheral aberration caused by the front lens of the objective not being itself achromatised. They are classified 1, 2, 4, 8, 12, 18, and 27, according to their magnifying powers. They can also be employed with other objectives. They consist (1) of **search oculars or finders**: (2) the **ordinary working oculars**; and (3) **oculars for projection.**

[1] In the construction of lenses having these properties they were greatly aided by the Messrs. Zeiss. The German Government paid them the handsome subsidy of £3000 for the right to the discovery. A large manufactory has lately been established in Jena for the production of optical glasses, known as the Glastechnische Laboratorium, Schott and Genossen.

53. **On Choosing a Microscope.**—In procuring an efficient instrument, a great deal depends, of course, on the object for which it is to be used, and the money which the purchaser is willing to expend upon it. If a microscope is required merely for ordinary histological purposes, it can be procured, of excellent quality, from £6 to £8; but if a series of higher lenses is desired, and a stand with an achromatic condenser fitted to it, then the purchaser should make up his mind for an outlay of from £20 to £30 at the least.

The instrument which is most convenient for ordinary working should have a small plain stand, with as few fittings about it as possible, and be provided with an ocular and objectives in which the low power objective magnifies 40 to 50 diams. with the tube in; while the high power should magnify 300 diams. with the tube in, and 350 to 400 diams. with it drawn out. It is a mistake, and one which beginners very often make, to suppose that very high magnifying powers are necessary for ordinary pathological work. There has been more pathological investigation done with the above enlargements than with any others, and the author would specially caution beginners from adopting the use of very high lenses at first. It is, in reality, more for bacteriological work that a magnifying power over 350 diams. is required, than for ordinary pathological histology.

Excellent cheap working microscopes of this range have long been made by Continental opticians, among whom Hartnack, Zeiss, and Leitz can specially be recommended; and in this country there has been a strong effort made of late to turn out a similarly cheap and good instrument. It is to be regretted, however, that our English microscopes of this class are as a rule inferior in several points as compared with those of Continental makers. They usually do not possess the requisite magnifying powers—being either too high or too low. The fine adjustment is very frequently deficient in steadiness or in length of available thread of the screw, and, moreover, it sometimes happens that while the middle part of the thread is steady enough the ends are totally untrustworthy. Then, again, there is much less equality in the lenses supplied by several English firms than there is with those, for instance, of Hartnack of Potsdam, or Zeiss. Messrs. Beck have of late turned out an instrument, "The Star," which is a great improvement upon anything of the kind they had before, and, certainly, for the money (£2:2 to £5:15) it is perhaps as cheap a microscope as is to be had. It is a pity, however, that they do not expend a little more care upon the lenses, especially the low power, and make the microscope correspondingly dearer, as one would rather give a little more in order to be sure of a first-class article. Messrs. Swift and Crouch both supply a cheap microscope suited for histological work, and some of their lenses are excellent in quality. Never buy a cheap English microscope, however, it matters not by what firm it is made, without having it thoroughly overhauled by some one competent to judge, and without comparing it with a similar microscope, say of

Hartnack or Zeiss. Cheapness is only one recommendation; uniformity in the quality of the instrument is much more important.

The author usually works with Hartnack's microscopes, and has invariably used them in his class. He can hardly recall a single instance in which the fine adjustment has got out of order, and has found the lenses, with few exceptions, of uniform and excellent quality. The microscope, No. IIIA in the catalogue, provided with Nos. 3 and 7 objective and Nos. 3 and 4 ocular, can be had for £7 : 10. Without the mahogany box, and with only the No. 3 ocular, it can be had for about £5 : 5. In reality, the latter furnishings are what are required in a class of pathological histology.

If a more expensive instrument is to be purchased care should be taken, in the first place, that it is provided with the before-mentioned powers for ordinary histological work. It should, in addition, have an oil immersion magnifying from 600 to 900 diams., and an achromatic condenser to use with this. As regards a stand, our home workmanship is undoubtedly quite as good if not superior to that of Continental makers. The "Pathological Stand" of Messrs. Beck, and also those recently brought out and adapted for bacteriological work by Messrs. Swift and Baker, on the pattern designed by Mr. Nelson, can be specially recommended. These may be fitted up with the makers' own lenses or with those of some other firm. The high lenses made by Beck, and Powell and Lealand, in this country, are not surpassed anywhere, and if one is willing to give the money for them, there is a certainty of possessing an article which cannot well be improved upon. Zeiss of Jena makes very beautiful oil immersion lenses, but they are quite as expensive as those of the best English makers. Leitz turns out oil immersions which are very much in favour in Germany at the present time. They are extensively employed for bacteriological work, and are remarkable for their clearness of definition and their cheapness. They are perhaps the cheapest oil immersions of the same quality to be had anywhere. Hartnack has a beautiful $\frac{1}{12}$ oil immersion that can be thoroughly trusted. The author has lately seen the $\frac{1}{12}$ oil immersion of Messrs. Swift and Son, costing £5 : 5s., and can highly recommend it for bacteriological work. A student provided with a Swift's improved Nelson's stand and nose piece, furnished with either an Abbe or a wide-angled achromatic con-

FIG. 19.—BECK'S PATHOLOGICAL STAND.

denser, and his medium eye-piece A or B, together with a No. 4 new series Hartnack dry objective, would be admirably equipped for bacteriological work. The cost of such a combination would be not more than £16 to £18.

Any of these makers, in fact, will furnish an oil immersion admirably suited for bacteriological work. There is less danger in choosing one of these than there is in selecting lenses which are cheaper.

54. **Testing a Microscope.**—First examine the stand as regards stability. If it shakes at all, or if there is any danger of its being upset, it should be rejected. Remove the eye-piece, look through the tube with the low power objective on, and see whether the openings in the diaphragm are all central. Readjust the eye-piece and put on the objective magnifying 300 diams. Place a preparation in focus, and notice if there is any lateral motion when the fine adjustment is brought into use. Do not try simply the middle part of the thread of the screw, but move it up and down to its extreme limits. If there is lateral motion of the field at any point of the fine adjustment, the stand is unhesitatingly to be rejected. If a rack is the means of coarse adjustment, see that it glides quite easily without the slightest hitch.

The field should be large with all the lenses. In pathological microscopes this is of the utmost importance, and it is here that most cheap lenses fail. The field is stopped down with a small eye-piece diaphragm so as to cut off the aberrant peripheral rays which are so difficult to correct, and, hence, if a microscope has a very small field it is a pretty sure sign that the correction for spherical or chromatic aberrations is faulty. If when a perfectly flat object is looked at, the peripheral part of the field is not in focus at the same time as the central, it has not been properly corrected for *spherical aberration* and should be rejected. If a number of coloured circles are seen at the edge of the field, and if objects examined appear coloured, it has not been properly corrected for *chromatic aberration*, and ought similarly to be rejected. Want of flatness in the field, and failure to correct the unequal refrangibility of the rays entering into the composition of white light, are two of the commonest faults in a cheap microscope. The field ought to be perfectly flat, even where it is large, if the eye-piece and objective are properly adjusted.

These matters having been settled, the next point to examine is the definition. At present, the author is recommending a microscope which will be suitable for histological purposes, and the best test-objects to examine are neither the scales on the wings of lepidoptera, nor the markings on diatoms, but an actual preparation such as is going to be the main object of observation afterwards. The most trying test for a histological microscope is a thin section of a delicate tissue, such as a very fine meshed scirrhous tumour of the mamma, mounted in Farrants' medium. If the microscope is possessed of the qualities requisite for the pathologist, such a preparation will bring them out

at once. Place it side by side with a microscope of known excellence and compare the two. It will be found that with such a test-object, those objectives of medium or low angle of aperture give a far more brilliant definition than those of wide angle. Their power of penetration is superior.

With an oil immersion lens, perhaps the best tests are also the objects which are to be chiefly examined with it, namely, stained bacteria mounted in Canada balsam. The spores in the tubercle and anthrax bacilli are excellent tests for very high ($\frac{1}{18}$) or medium immersions ($\frac{1}{12}$). In both cases they should be clearly defined.

55. **Drawing of Microscopic Objects.**—Several simple devices may be adopted for this purpose. Thus, if the microscope be placed horizontally, and a small piece of thin glass be fixed at an angle of about 45° to the surface of the upper lens of the eye-piece, an image of the body will be seen on a sheet of paper lying at a distance of ten inches below, when the eye is placed directly above the piece of glass. The rays are reflected upwards to the eye from the glass, and give the impression as if the image lay upon the paper. A piece of polished steel or a prism has a like effect, and Beale recommends a piece of neutral tinted glass as being easier to draw from than one which is uncoloured.

Many simple instruments are to be had made on this principle. They will, however, be found to be rather awkward to work with, owing to there being some difficulty in keeping the image of the object and the point of the pencil simultaneously in view.

A more ready means of drawing an accurate outline of any object is what is known as *Oberhauser's or Chevalier's camera lucida.* This instrument is convenient from the fact of its being used with the microscope in the upright position. The ordinary eye-piece is removed, and the camera substituted for it. In the upright piece which passes into the tube of the microscope, a prism is so arranged that the light passing up through the microscope is deflected by it at right angles into the horizontal part of the instrument. In this horizontal piece are placed the two lenses of an eye-piece, and at the extreme end of the eye-piece, again, is a small prism set in a black ring, which reflects the image up to the eye of the observer placed above. The whole instrument is, essentially, merely an eye-piece placed at right angles to, instead of in the axis of, the microscope, with an enclosed prism to turn the rays into it. The object of this is to do away with the inconvenience of having to keep the microscope inclined. The essential part of the instrument is, of course, the small prism at the end.

This camera is just as difficult to work with as the simple piece of glass, unless arrangements are made to darken the surroundings. It then becomes so easy to employ, that a person quite unaccustomed to draw can readily make a correct outline of any desired object. It should be placed in a dark chamber, in the shutter of the window of which two small apertures are bored, so that the light from the one

falls on the mirror of the microscope; that of the other upon the point of the pencil. The paper is placed at a distance of ten inches from the end prism as before. The difficulty of simultaneously seeing the object and the point of the pencil will thus be found to have entirely vanished.

Abbe's Camera Lucida.—This instrument made by Zeiss must be specially mentioned. The advantages it possesses are that the image is neither distorted nor magnified by the camera, and, at the same time, the image and the pencil are seen coincidently without any straining of the eyes.

56. **How to determine the Magnifying Power of a Microscope.**—Procure a stage-micrometer with a scale engraved upon it in fractions of an inch or millimètre. In English stage-micrometers the subdivisions are usually in thousandths of an inch; in French and German micrometers, on the other hand, the subdivisions are almost always in hundredths of a millimètre. Either scale will answer the purpose, provided that the engraving has been done with accuracy. Opposite every fifth interspace in the millimètre micrometer the line engraved on the scale is longer than in those intermediate, while opposite every tenth interspace the line is longer still. By this means five or ten interspaces can very readily be counted off.

Suppose that it is an ordinary Hartnack microscope which is being tested. Set it in the upright position, first with the upper tube in, and with, say, the No. 7 objective and the No. 3 ocular. Bring the scale engraved on the millimètre stage-micrometer into view. Place a sheet of white paper at a distance of ten inches from the eye of the observer, that is to say at the normal distance for clear vision. The small Hartnack stand is exactly this height, so it will suffice to lay the paper on the table.

Look through the microscope with both eyes open, and half of the scale will be seen on the white paper, half will appear to be within the microscope. With a pair of compasses held against the paper, or simply by marking with a pencil, measure off ten interspaces. These ten interspaces are equivalent to a distance of ·1 millimètre, and it remains to be seen how much this distance has been magnified. Compare the interval between the blades of the compasses with an ordinary millimètre hand measure. With the magnifying power we have presupposed, it will probably be found that it equals thirty millimètres. This number must now be divided by the actual distance magnified, namely, ·1 millimètre, and the quotient, 300, will be the linear magnifying power of this combination. In fact, if ten interspaces are taken, it will be evident that all that is necessary in order to get the magnifying power of the microscope is to add a cipher to the number of millimètres to which the distance between the points of the compasses corresponds on the scale.

The magnifying powers of the microscope, with the upper tube half out and with it completely withdrawn, should be similarly tested, and a

record kept of each result. Care should be taken to alter the position of the paper so as to ensure that the normal range of distinct vision (10 inches) is maintained between the eye of the observer and the points of the compasses.

57. **Measurement of Microscopic Objects.**—Several means may be adopted for this purpose. The most direct is to employ the stage-micrometer as a slide for mounting the object upon. If blood for instance, is under examination, a preparation is made of it on the stage-micrometer, and the size of the corpuscles is directly compared with the divisions on the scale. This method, however, is now seldom used, as, in the first place, it is inconvenient; and, in the second, the markings of the scale become obliterated from the constant friction in cleaning the slide, as well as from being filled with the medium employed in mounting.

By far the readiest method is to measure the object by means of an eye-piece micrometer. An eye-piece micrometer is an ordinary eye-piece into which a round piece of glass is inserted immediately above the diaphragm, and on which a series of equidistant lines is engraved. These lines are marked off by the greater length of certain of them, into groups of five and ten, so as to be more easily counted. The distance between the lines must be equal, but no one standard of size need be universally adopted. What is required is that the spaces between the lines be not too wide, and that they be perfectly equidistant.

In employing this scale in estimating the size of a body, it is necessary, firstly, to find what the value of each space is with the particular lens which is being used. For this purpose a *stage-micrometer* in which the breadth of the spaces between the lines is known, must be compared with it. In order to do so, the stage-micrometer is brought into focus, and the lines engraved upon the eye-piece micrometer are placed parallel with those upon it. Let us employ a stage-micrometer in which a millimètre is subdivided into hundredths, and let us suppose that the Hartnack's No. 7 objective with the eye-piece micrometer of the same maker are used for conducting the observation. It will usually be found that with this combination one of the spaces in the stage-micrometer is equivalent to three of those in the eye-piece. As the spaces of the stage-micrometer are of the value of the hundredth part of a millimètre, each of those in the eye-piece must correspond to a third part of this.

The micrometer spaces = ·01 millimètre.
The eye-piece spaces = ·01 ÷ 3 millimètre.
·01 mm. ÷ 3 = ·0033 millimètre.

The thousandth part of a millimètre is known among histologists as a *micromillimètre*, and is expressed by the Greek letter μ. The value, therefore, of each space in the eye-piece micrometer is equivalent to $3{\cdot}3\mu$.

Let the body to be examined be a salivary corpuscle. How do we proceed? A preparation of it is substituted for the stage-micrometer, and a single corpuscle is brought under the lines of that within the eye-piece. Suppose that the diameter of this corpuscle covers three of the spaces, then as each space is equivalent to $3{\cdot}3\mu$, the diameter of the corpuscle will be $9{\cdot}9\mu$. Measure another, and probably it will be found to occupy five spaces. Its diameter will then correspond to $3{\cdot}3\mu \times 5$, or $16{\cdot}5\mu$.

If the value be desired in a fraction of an inch, this can be got by directly converting the result obtained by the above method, or by the use of a stage-micrometer in which the inch is taken as the standard. The manner of going about the measurement is alike, namely, to find by the use of the stage-micrometer what the value of the spaces in the eye-piece is, and then seeing to how many of these the body corresponds.

Accessories to the Microscope.

58. The following are absolutely necessary, although many others may be procured in course of time. It will be found, however, in working, that many of the accessories often recommended are comparatively useless.

(1) Two pairs of strong straight needles set in wooden or ivory handles.

(2) A pair of flat slightly curved scissors and a small pair of straight ones.

(3) A small scalpel, or, what is better, if at hand, a complete dissecting case.

(4) Three or four dozen slides with ground edges, 3×1 inch.

(5) Three or four dozen slides with ground edges, $3 \times 1\frac{1}{2}$ inch.

(6) Thin round cover-glasses to suit.

(7) A reagent stand capable of holding from six to twelve bottles. The bottles should have rods attached to the stoppers. The stoppers may be made either of glass or cork.

(8) A white porcelain slab about 9×9 inches, and a piece of ground plate-glass, blackened behind, of the same size.

(9) Two small white basins filled with water.

(10) A few small goat's-hair brushes.

(11) A turning table.

(12) A cabinet capable of holding several hundred slides. If the preparations are to be carried about, it is better to be provided with several small cabinets instead of a single large one.

(13) Labels for slides.

(14) Test glasses and test tubes.

(15) Half a dozen small porcelain evaporating dishes. These are preferable to watch-glasses, which are very liable to be upset.

(16) Several small pipettes and some glass tubing for drawing out into pipettes, injecting nozzles, etc.

(17) A nest of glass beakers, and a dozen small beakers of about half an ounce capacity.

(18) A bell-jar.

(19) A few small glass rods.

(20) Filter paper.

(21) Towels and soft old washed linen rags for cleaning cover-glasses and lenses.

(22) A number of wide-mouthed stopper bottles.

(23) A razor, or what is better, a flat brain-knife similar to that used in making *post-mortem* examinations. These are useful for cutting a rough and ready small section of a tissue in order to examine its condition during the process of hardening, etc. They are not to be recommended for making permanent sections.

(24) A spirit lamp or small Bunsen burner.

(25) A twenty-ounce bottle of methylated spirit and a ten-ounce bottle of absolute alcohol.

(26) Stricker's warm stage for examining small living objects at a given temperature. The instrument is so arranged that by heating a copper wire in front with a spirit lamp, the temperature of the stage, which is indicated by a thermometer, can be kept pretty constant. A tube is provided at each side for the introduction of gases, if required, into the well of the stage. To use it, anoint the edge of a thin cover-glass with vaseline and place the drop of liquid, blood, etc., in its centre. A second cover-glass is slipped over this and gently squeezed so as to spread the vaseline. The cell thus formed is now fixed on the stage and examined. If the bodies under examination are intended to be acted on by gases the lower cover-glass is omitted.

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59. **Pathological Photography.**—The present work is quite unsuited for entering into the details of a subject so vast as that of photography. The author has consequently limited his remarks to quoting some of the more recent works treating of microscopic photography and photo-micrography. Every pathological laboratory should be fitted with a dark room and other arrangements for photographing. Naked-eye objects, as pointed out by Gourley, photograph much better when pinned on a black board and submerged in water.

Printing in colour is done by the Autotype Company, London, and by Römmler and Jonas of Dresden.

As a general guide Captain Abney's work on *Instruction in Photography*, 1886, and Hardwick's *Manual of Photographic Chemistry*, edited by Taylor, 1883, may be consulted. Other recent treatises are the following:—

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CHAPTER VIII

PRACTICAL BACTERIOLOGY

GENERAL REMARKS

60. BEFORE a particular micro-organism can be held to be the actual *materia peccans* of a disease it must (1) be found in the affected tissues or in some other part of the body; (2) it must be capable of isolation, and of being cultivated artificially; (3) the artificial culture must be proved to reproduce the disease; and (4) the organism must again be discovered in the body of the inoculated host.

One of the main objects of practical bacteriology is the perfection of methods whereby these criteria may be fulfilled.

ARTIFICIAL CULTURE MEDIA.

61. Of these there are two varieties—*liquid* and *solid*. Some years since liquid media were almost exclusively employed. Since the introduction of gelatine as a culture basis by Koch, however, solid media have almost entirely supplanted them, unless for particular purposes, such as the cultivation of an isolated organism in large quantity, or where the products of germ growth (ptomaines, etc.) are to be the object of study. Solid media are preferable to liquid for the *differential* cultivation of most micro-organisms (1) because several can be grown side by side in the same mass without their intermingling; and (2) because the manner in which they grow on the solid surface is an important diagnostic indication of their nature.

(α) *LIQUID MEDIA.*

62. (A) **Bouillon.**—This is one of the most useful, and may be made from the muscle of the ox, sheep, chicken, etc. That made from ox muscle will usually be found to be suitable for the growth of most organisms. It is well, however, to select the muscle of the same kind of animal as that which has contracted the disease under observation.

Bouillon contains the extractives and salts of the meat, and, after prolonged boiling, probably some soluble albumin. As the amount of organic matter in it is small, it cannot be expected to support an active growth for any length of time. The meat from which it is made should be as fresh as possible, seeing that it becomes acid by keeping, and is, moreover, liable to be contaminated with foreign organisms to a greater extent than is avoidable with ordinary precautions.

Procedure.—Mix 500 grm. of lean meat, free from fat and finely chopped, with 1000 c.c. distilled water. Allow the mixture to stand in ice for twenty-four hours. Boil for about three-quarters of an hour and carefully filter, first through muslin, subsequently through paper. The reaction will probably be acid, and as the majority of vegetable micro-organisms grow best in a neutral or faintly alkaline medium, it must be neutralised by addition of solution of sodic carbonate. All artificial media, whether solid or liquid, must be similarly neutralised.

The neutralisation is to be effected with the utmost care so as not to overstep the neutral point. It is better, however, to err on the alkaline than on the acid side.

If the liquid contain excess of alkali it may become turbid from precipitation of phosphates. Should this happen the alkalinity is to be corrected by the addition of lactic acid, with subsequent reboiling and filtering. A very small quantity of lactic acid is usually sufficient. Should it still remain turbid the addition of the white of an egg to the beef tea while it is cold, with subsequent prolonged boiling, will render it perfectly limpid.

(B) **Pasteur's Fluid.**—This consists of the following ingredients (No. 312, lviii. p. 323):—

Tartrate of ammonia .	1 grm.
Candy sugar . . .	10 „
Distilled water . . .	100 c.c.
The ash of 1 grm. yeast.	

(C) **Cohn's Fluid** (No. 355, i. 2 Heft, p. 195) is composed of—

Phosphate of potash . .	0·5 grm.
Crystallised sulphate of magnesia	0·5 „
Tribasic phosphate of lime .	0·05 „
Distilled water . . .	100 c.c.

Then dissolve in it 1 grm. tartrate of ammonia.

Pasteur's and Cohn's Fluids, besides being media on which many pathogenic and other bacteria may be cultivated are particularly serviceable for the growth of the moulds. Pasteur's fluid is supposed to supply synthetically the elements necessary for the support and increase of the lower fungi. As a medium for the growth of bacteria, however, it is inferior to the albumin and albuminoid containing preparations so much in use at the present day. Of all forms of a purely

carbonaceous pabulum on which low vegetable organisms will grow, *grape sugar* probably supplies the most readily assimilable, while *albumin* is to be regarded as best adapted when carbonaceous and nitrogenous elements combined are desired, more especially if in the form of peptone (Nägeli, No. 356). A mixture of the two will, therefore, probably afford the richest available nourishment.

(β) *SOLID MEDIA.*

63. (*a*) **Koch's Nutritive Gelatine** (No. 44, i. 1881, p. 24). Of all nutritive media in use at present this is undoubtedly in most favour. It is made by mixing 500 grm. finely chopped lean meat, free from fat, with 1000 c.c. distilled water. The meat is allowed to soak in a cool place for twenty-four hours, and if the weather be warm it should be placed in an ice safe. The red coloured liquor is filtered off through muslin after this, and the meat is squeezed in the hands or in a screw-press so as to get as much juice out of it as possible. If the liquor does not come up to 1000 c.c. (the original quantity) some more distilled water is to be added to the meat, stirred up with it, and again filtered off until the requisite amount has been obtained.

FIG. 20—MEAT-PRESS FOR EXTRACTING BEEF-JUICE.

To this have to be added—

10 grms. colourless peptone,
5 „ common salt,
and 100 „ French gelatine in flakes.

The gelatine should be cut into strips, and must be allowed to soak for at least fifteen minutes in the liquor before being melted.

The whole is now heated in a steam steriliser (Sect. 69) so as merely to melt the gelatine (about 65° F.) but not to precipitate the albumin of the meat. It must then be neutralised as before directed (Sect. 62), and boiled for an hour. Great care must be exercised not to overstep the alkaline turning point to any great extent, otherwise there may be some difficulty in clarifying the medium.

Filtering.—It is filtered through paper while hot, a warm water funnel being employed if there is any difficulty in getting it to pass, a proceeding which, as a rule, is unnecessary. All that is usually needful is an ordinary funnel provided with Swedish filter paper, and thrown into a sufficient number of folds.

The warm water funnel consists of a copper casing, into which an ordinary funnel can be fitted water-tight by an india-rubber cork

surrounding its neck. Water is poured into the interval between the two, and is heated by a Bunsen burner, either through a projecting arm or by means of a circular fringe of small gas jets.

As the medium is being boiled, the albumins are precipitated in the form of a thick tenacious mass. If the neutralisation has been carefully conducted they are usually sufficient to carry down any impurities with them, and to render the liquor quite clear. If it still remains muddy after filtering, the white of an egg ought to be shaken up with it at as low a temperature as is consistent with the medium remaining liquid, the whole being subsequently reboiled and filtered.

FIG. 27.—ROHRBECK'S FILTER FOR NUTRITIVE GELATINE.

Use of Various Ingredients.—The constituents of the meat which are retained in the mixture are mainly its *salts* and *extractives*. It is always better to derive these from their natural source than to attempt to compound them synthetically.

Peptone is employed with the view of supplying a proteid basis which will not coagulate by heat. Bacteria convert albumin into peptone before assimilating it, hence another reason for its employment.

The addition of *common salt* aids the solution of the peptone.

The *gelatine of commerce* probably differs somewhat in composition. It seems, however, to be mainly a mixture of chondrin and mucin. Some bacteria have the property of liquefying it, others have not. Those which liquefy probably secrete a *ferment*. It should always be employed of the same proportional strength (10 per cent), as the manner in which various bacteria grow depends to some extent on its solidity. If too much alkali is employed in neutralising, and more especially if, in addition, it is subjected to prolonged boiling, it is apt to lose its gelatinising properties.

(*b*) **Agar-agar Medium.**—The above gelatine basis is admirably suited for the growth of bacteria at the ordinary temperature of a sitting-room. Where a higher temperature is requisite, gelatine cannot be employed, as it liquefies, and *agar-agar*, or some other substance which melts at a higher temperature than gelatine, must be substituted.[1]

Its solution is aided by soaking over night in salt and water, the salt being afterwards removed by successive washings before being used. The same ingredients, with the exception of the gelatine, are employed as in Koch's medium. The proportional quantity of agar does not

[1] Agar-agar is a vegetable gelatine obtained from several sea-weeds on the coasts of Japan, India, Ceylon, etc. It melts at 90° C., fixes at 40° C., and boils at 105° C.

require to be so great. It will be found that 10, 15, to 20 grm. per 1000 c.c. is sufficient to furnish a firm jelly. A little liquid is usually squeezed out of the mass as it cools. The jelly remains solid at the highest temperature that may be employed for culture purposes. It ought to be boiled for an hour, neutralised, and clarified with the white of an egg as before described.

While liquid, it is perfectly limpid and transparent, but as it cools it always becomes slightly milky.

On account of this opacity Edington (No. 59, 1886, ii. p. 704) substitutes Irish moss for Agar-agar. It possesses greater transparency, and is of itself an excellent culture basis. Two ounces of moss are soaked over-night in eighteen ounces water. Next morning the swollen moss is boiled in the steam steriliser for an hour and a half, and is shaken up from time to time. The mass is then pressed two or three times through flannel or felt, and a clear liquid is thus obtained which gelatinises at 31° C. If the liquid is evaporated down to ten ounces and gelatinised, it melts at 50° to 55° C. It may be mixed with 2 per cent peptone and 1 per cent cane sugar.

(*c*) **Solid Blood-serum.**—There are some organisms which will not grow, or which grow with the greatest difficulty, on the gelatine media just described (*e.g.* tubercle). It was discovered by Koch (No. 43, xix. 1882, p. 224) that blood-serum when partially coagulated fulfilled the purposes of a solid gelatine medium, and afforded a nutrient basis on which many of these refractory organisms grow luxuriantly.

Source.—The blood-serum may be obtained from various animals, the ox being that which is generally chosen. Several wide-mouthed stopper-bottles are sterilised by rinsing them thoroughly with solution of corrosive sublimate (1 to 1000). The sublimate is removed with alcohol; and in order to facilitate the drying of the interior of the bottles the alcohol is washed out with ether, which is allowed to evaporate while the mouth of the bottle is held downwards. The stopper is replaced and rendered air-tight with vaseline.

As the animal is being bled from the aorta or innominate, the first gush of blood is rejected as probably being impure. The stopper is carefully removed in course of time, with the mouth of the bottle downwards, and each bottle is about three-fourths filled with blood. The stopper is immediately replaced, and all the bottles similarly filled are placed for twenty-four hours in a trough filled with ice, so as to hinder coagulation, and prevent the growth of any bacteria or their spores which may have accidentally gained access. As the clot begins to get firm (two to three hours afterwards) it is well to separate it from the sides of the vessel with a sterile glass rod, so as to allow of the blood-serum being pressed out. If this is not done it may happen that comparatively little serum will be obtained by the following day.

Sterilisation.—The blood-serum, as free as possible from corpuscles, is now introduced by means of a sterile pipette into test-tubes which

have been previously plugged with cotton and sterilised (see p. 122). They are immediately afterwards placed in a *serum-steriliser* in the upright position and heated to from 54° to 56° C. daily for two hours on eight successive occasions. The object in doing so is to sterilise any impurities which may accidentally have gained entrance.

The serum-steriliser consists of a double-walled round chamber, the interspace between the walls being filled with water. The lid is similarly constructed, and is perforated with an aperture for a thermometer. The interior of the chamber is subdivided by partitions into four compartments for the reception of the test tubes. The body of the chamber is heated by a Bunsen burner below, the lid being heated by another burner, placed under a hollow arm projecting from its side. The temperature can be regulated by a thermostat.

FIG. 28.—ROHRBECK'S APPARATUS FOR STERILISATION AND STIFFENING OF BLOOD-SERUM.

Koch employs one apparatus for sterilising blood-serum and another for stiffening it. There is no reason, however, why both processes should not be carried on in the same chamber. Rohrbeck manufactures an apparatus for this purpose.[1]

Stiffening.—When sterilised, the tubes are laid in the serum-stiffener at a temperature of 68° C. The *serum-stiffener* is a double-walled four-sided box, with water in the interspace, as in other like instruments. It is set upon legs, two of which, at one side, can be raised or lowered by removable screws, so as to incline the apparatus at any desired angle. A thermometer is laid on the floor of the apparatus side by side with the tubes. A thermostat may be inserted as in the serum-steriliser.

[1] This and all other bacteriological apparatus can be had from Dr. Rohrbeck, 24 Karlstrasse, Berlin, at very moderate cost. Messrs. Becker & Co., 34 Maiden Lane, Covent Garden, London, also furnish most of the instruments used in Professor Koch's laboratory.

In course of time the liquid serum solidifies into a somewhat opalescent jelly, which forms an admirable culture surface.

After-treatment.—As soon as the contents of a tube are noticed to have become solid the tube is removed. The tubes, covered with caoutchouc caps, are afterwards retained at a body temperature in an incubation chamber (see Sect. 76) for several days. A little liquid always exudes from the mass. If this becomes turbid, or if opaque spots or flakes are noticed in the jelly, then the tube is impure and ought to be rejected.

FIG. 29.—KOCH'S SERUM-STIFFENER.

Unna's Method of preparing Blood-Serum.—Owing to the low temperature which can alone be employed for the sterilisation of blood-serum, the process is necessarily protracted and never quite certain. Unna (No. 48, iii. 1886, p. 521) has devised the following procedure in order to overcome these difficulties. About 40 c.c. of blood-serum from the calf are poured into a large vessel, and to this about half the quantity of binoxide of hydrogen (H_2O_2) is added drop by drop, shaking the vessel meanwhile vigorously. The binoxide should be dropped in until the brown scum which gathers on the surface becomes white. The mixture, which is now acid, is rendered slightly alkaline with a two per cent carbonate of soda solution. It is next filtered through a funnel lined with a double layer of paper one quarter filled with well-calcined "Kieselguhr." Whenever the liquid comes through clear it is allowed to run directly into the test tubes. The latter are then placed in a Koch's blood-serum stiffener, whose interspace is filled with oil instead of water. The oil is heated up very slowly, the flame being removed whenever a whitish cloudiness is noticed in the serum, as the coagulation point is reached. The advantage of adding the ingredients above-mentioned is that they enable the serum to coagulate at a much higher temperature than it does naturally (90° to 120° C. in place of 65° C.). When coagulation is completed, the temperature at which it has taken place is maintained for an hour. The water of condensation is poured off, and the tubes are retained for another half-hour at the same temperature. The water of condensation is again removed, and the warm test-tubes are transferred to a steam steriliser at about 60° C., in which they are slowly heated up to a boiling-point, or retained at this for quite half an hour.

If an excess of carbonate of soda be added, the serum will fail to coagulate even at the above high temperature.

Neither the binoxide of hydrogen nor the carbonate of soda interfere with the serum as a culture basis.

(*d*) **Glycerine Agar-agar.**—This can be substituted for stiffened blood-serum in the cultivation of the tubercle bacillus.

Dr. Crookshank informs the author that he has entirely given up blood-serum for the above purpose, finding that glycerine agar-agar is so much more readily prepared, and forms an equally good culture basis. It is made simply by adding 6 per cent glycerine to the ordinary agar medium.

(*e*) **Sterilised Potato.**—For the cultivation of *chromogenous bacteria*, or such as secrete a colouring matter, there is no better basis than sterilised potato. It may happen, as in the case of the glanders bacillus, that when sown on nutritive gelatine the organism appears to be colourless, whereas on potato its chromogenic properties assert themselves.

A potato surface is also useful *as a means of encouraging certain organisms to spore.* Thus anthrax, if sown on this basis and kept in the culture chamber, will be found to be sporing prolifically within forty-eight to sixty hours.

The older method of preparation consisted in placing an entire half of a sterile potato in a moist chamber. A more convenient method is to keep only little blocks of it in glass capsules provided with loose lids (Esmarch).

The potato is scrubbed with a hard brush under a stream of water. It is then left in a solution of corrosive sublimate (1 to 1000) for an hour or so to purify the surface. With a knife rendered sterile by passing it through the flame of a Bunsen lamp, a quadrilateral piece is cut from the centre, and is rapidly transferred to the glass capsule previously sterilised by heat. The capsules with contained potato are next placed in the steam steriliser, and the sterilisation is completed, as elsewhere described (Sect. 69). The potato, even although the lid covering it fits comparatively loosely, will remain free from contamination and ready for inoculation for months, more especially if the capsules be protected by a bell jar.

Inoculation.—Lift the lid of the capsule half up, and with a sterile öse, or with a platinum needle having some of the culture to be inoculated adhering to it, scratch a number of lines upon the surface of the potato. This may be done in the greater number of instances without contamination, if ordinary precautions are observed (Sect. 75).

Potato Paste may be substituted for the solid potato when a very extensive surface is desirable. The potatoes are boiled for an hour, and the dry floury centres are mixed with sufficient distilled water to convert the whole into a stiff paste. This paste is enclosed in suitable glass capsules, and sterilised with steam in the usual manner (Sect. 69).

(*f*) **Bread Paste.**—Stale coarse bread is thoroughly dried in an oven, but not roasted. It is ground to powder in a mortar, and moistened with distilled water sufficient to convert it into a paste. It is then placed in the sterile capsules used for potato, just described, and is sterilised in the steam steriliser in the usual manner (Sect. 69). It has an acid reaction, and is particularly well suited for the growth of moulds. If it is to be employed for the culture of bacteria, it must be neutralised with solution of carbonate of soda.

Culture-Tubes.

64. Ordinary test-tubes of a quarter, half, or three-quarter inch diameter are the most convenient.

McFadyean (No. 6, 1888, i. p. 304) has devised a very ingenious tube for the purpose of inoculating liquid media with the mouth of the tube downwards. It consists of an ordinary test-tube, with an arm coming off from one side. The liquid is run into the arm during the time of inoculation, and, on reversing the tube, after the inoculation is completed, it flows back again.

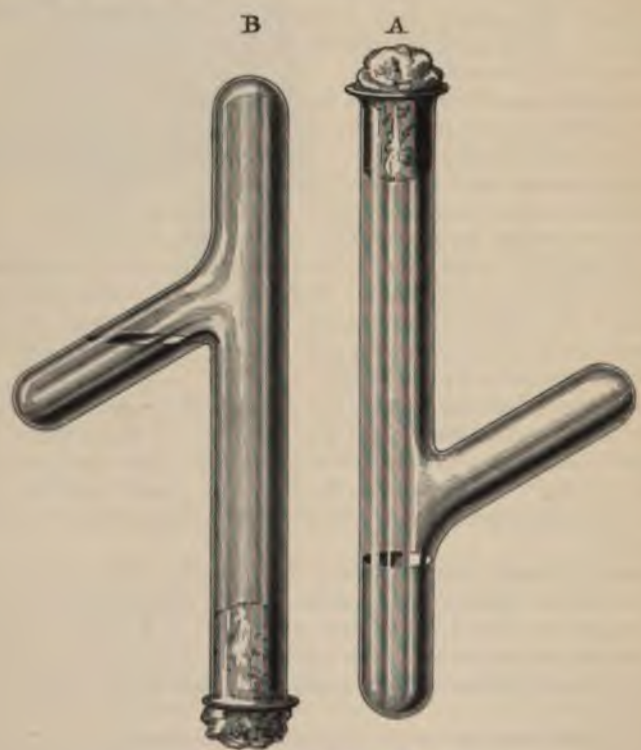

Fig. 30.—McFadyean's Tube.

Preservation of Culture Media.

65. The various media can be retained if desired in sterile flasks until required. It is much better, however, to decant them into the tubes in which the cultures are to be made. The medium is poured into these through a small funnel after they have been sterilised. Each tube should be about one-third filled. The tubes and their con-

tents are then sterilised with steam (Sect. 69). It is sometimes advisable to make a surface culture on the gelatine, in which case the gelatine should be allowed to solidify with the tube in the prone position.

The cotton which plugs the tubes must be kept quite **dry,** otherwise it loses its germ-filtering properties. When the tubes have been proved to be sterile, the superfluous part of the plug is cut off and the cut surface is singed in a Bunsen flame, while the neck of the tube may be heated at the same time, so as to sterilise it, if by chance any contamination have taken place. A caoutchouc cap is finally adjusted

FIG. 31.—LISTER'S FLASK: N, the bulb; P and C, cotton plugs; O, nozzle.

over the end of the tube. The tubes may thus be retained ready to inoculate for almost any length of time.

Lister's Flask.—Where it is desired to take a small quantity of sterile liquid from time to time out of a vessel, this may be employed with advantage.

It consists (No. 192, xxix. 1878, p. 430) "of a flask (N, see fig. 31), having a bent spout, large at the commencement and comparatively narrow in its shorter terminal part (O) beyond the bend. The large size of the first part of the spout prevents it from ever acting like a syphon; and the result is that when liquid is poured from such a flask and the vessel is afterwards restored to the erect position, the end of

the nozzle remains valved by a drop of the liquid; and this guards the orifice, so that regurgitation of air can never take place through the nozzle. And the mouth of the flask being covered with pure cotton-wool (P), the air that enters the flask during the pouring out of the liquid is filtered of its dust by passing through the cotton. When the decantation is completed, a piece of rag wrung out of strong watery solution of carbolic acid (1 to 20) is applied to the orifice of the nozzle, and by capillary attraction sucks out the drop; after which a cap of carbolised cotton-wool (C) is tied securely over the nozzle, the ligature obtaining a purchase upon the projection (O) upon the tube. When this has been done, the liquid, if it was pure to start with, and the flask also pure, will remain ready to be used again in a pure condition a month or even a year later, if required."

Sterilisation of Vessels, Instruments, and Media.

66. Wherever vessels and instruments are of such a nature that they will withstand a temperature considerably over boiling point without injury, **hot air** is the means adopted to purify them. In the case of most instruments the sterilisation can be effected by simply holding them in a clear flame; but where large numbers of tubes, flasks, etc., are to be purified, a hot air steriliser is necessary.

Fig. 32.—Hot Air Steriliser with Sliding Screen on top to regulate the Air Circulation.

Koch and Wolffhügel (No. 44, i. 1881, p. 321) from their researches concluded that—

1. Bacteria free from spores are destroyed by hot air at a temperature of 100° C. after one and a half hours.

2. Spores of moulds require a temperature of 110° to 115° C. for one and a half hours for their destruction.

3. Spores of bacilli are killed by hot air at a temperature of 140° C.

4. The hot air penetrates so slowly into objects to be disinfected, that even after three to four hours at 140° C. bundles of clothing, etc., are not disinfected.

5. Heating at 140° C. for three hours injures most textile fabrics.

Gaffky and Loeffler (No. 44, i. 1881, p. 340) showed that disinfection with steam is not nearly so injurious to clothing.

67. **The hot air steriliser** is a round or four-sided chamber made of sheet-iron, and having a double wall. The outer wall of the bottom of the chamber is perforated by one or more large apertures, and the roof is perforated with a still larger number, the apertures in

the latter being capable of closure by means of a sliding screen, so as to regulate the air circulation between the walls. One, or it may be several Bunsen burners are used for heating it. There ought to be a few movable shelves inside, also made of sheet-iron; and an aperture, passing through both walls of the roof, communicates with the interior for the purpose of adjusting a thermometer. It may be placed on a basis of concrete, or suspended from a wall, a layer of asbestos intervening.

68. **Flasks and test-tubes**, before being sterilised should be firmly, plugged with cotton in such a way that the free extremity of the plug within the tube or flask is perfectly rounded and has no loose fibre adhering to it. All vessels are to be thoroughly washed, firstly, in ordinary water, and, lastly, in distilled. The superfluous water is allowed to run off, and they are plugged with cotton while damp. The test-tubes are placed in a wire crate, and care must be taken that the cotton does not touch the wall of the chamber, as otherwise it will become charred and brittle.

FIG. 33.—WIRE CRATE FOR HOLDING TEST-TUBES WHILE BEING STERILISED.

69. **Necessary Heat.**—Practically speaking it will be found that if glass vessels and cotton are kept at a temperature of 150° to 170° C. for half an hour they will be sterilised; in fact, if they have been in the hot chamber just until the cotton in some of the tubes begins to assume a yellowish-brown colour it will usually be sufficient. The cotton must, however, on no account be charred, otherwise it will become so brittle as to be useless as a plug and germ filter. The vessels may be left in the steriliser until the latter cools, although this is not necessary.

Sterilisation by Steam.—Liquid and solid media must be sterilised by steam. This prevents their becoming concentrated by evaporation, and the steam heat is also less liable to impair the stiffening properties of those which contain gelatine, or to cause decomposition of their ingredients.

The moist heat is much more effectual when *discontinuously* applied. Most bacteria are killed by a temperature below that necessary to coagulate albumin, and very few will withstand a temperature of 60° C. Their spores, however, may remain active at a temperature considerably above this. Tyndall's explanation of the efficacy of discontinuous sterilisation is that, during the intervals, spores become converted into rods, and that these are more readily destroyed by the heat. All culture media ought, therefore, to be discontinuously sterilised. On the first day, they are steamed for three-quarters of an hour to an hour, and, on the two succeeding days for from ten to fifteen minutes. The culture tubes will usually all be found to be sterile after this time. They should, however, be kept under observation for a week or more before

being used, in order to make sure that their sterilisation has been effectual.

70. **The steam steriliser** used by Koch consists of a large metal cylinder set on legs. It is covered with felt and has a tight fitting lid provided with an aperture for a thermometer, and with another to allow of the escape of the steam. At a depth of about 6 to 8 inches from the bottom is a movable metal grating. On this rests an inner tin vessel made like an ordinary pitcher, with a perforated bottom and a lid. The part of the cylinder below the grating is kept filled with water heated by a Bunsen, the depth of the water being indicated by a gauge. The tubes or other vessels containing media to be sterilised are placed in the pitcher, and are introduced when the water is boiling.

FIG. 38.—STEAM STERILISER (SURFACE VIEW).

FIG. 39.—STEAM STERILISER (SECTION).

FRACTIONAL CULTIVATION.

71. It usually happens that pathological liquids and tissues in their native condition contain several varieties of micro-organism, and in order to study their individual properties means must be taken for cultivating them separately. It is only thus that their characteristics can be investigated. The method by which the isolation is accomplished is known as *fractional cultivation.*

Brefeld and Nägeli are held to have originally suggested the procedure; but Lister (No. 192, xxix. 1878, p. 446) first put it to practical use, the organism which he isolated being the bacterium lactis.

The medium of attenuation was formerly sterile distilled water. Since Koch's introduction into Bacteriology of gelatinised media, however, these have been almost universally adopted. The advantage of a gelatinised medium is that when it is poured out in a thin layer, the organisms that may be present in it remain apart when growing, whereas, in a liquid, they become inseparably mixed.

The principle of **Brefeld and Nägeli's,** and of **Lister's method** was that of diluting a small portion of the virus with distilled water up to such an extent that, in all probability, only one organism would be contained in each drop. If successive drops be sown in a series of vessels containing a liquid culture medium, the chances are, provided the number of vessels be sufficiently large, that all, or nearly all, of the various organisms in the water will be obtained in a state of isolation and purity.

72. **Koch's procedure** consists in inoculating a tube of melted nutritive jelly with a very small quantity of the material in which the bacteria are contained. The gelatine is melted in a water-bath at as low a temperature as possible. The plug is withdrawn with care and a sterile platinum needle with the virus upon it introduced. The small particle of matter is thoroughly mixed with the gelatine by rolling the tube. Three drops of the gelatine are then transferred in succession on an öse (see Sect. 75) from this to a second tube, and so on similarly three drops from this to a third and fourth. The plug is carefully replaced in each case before the mixing commences. The "original" or first tube contains too many organisms to be of any use. Attenuation No. 1 is usually also to be discarded for a like reason; but Nos. 2 and 3 are to be reserved. In making the attenuations it is convenient to mark each tube by drawing out twisted horns of the cotton according to their order. The one is otherwise very liable to be mistaken for the other. The attenuation of the virus in the last tube must, of course, be very great, and it is from it that the best colonies can be obtained.

The next part of the *technique* consists in pouring the gelatine from the tubes over sterilised glass slips. A series of these slips somewhere about 5 × 2 in. in size are sterilised by placing them in a flat iron box with an easily adjustable lid. The iron box and enclosed slips are heated for half an hour in the hot-air steriliser up to 150° to 170° C. When cool, the box is removed and placed conveniently within reach.

FIG. 40.—IRON BOX FOR HOLDING GLASS SLIPS WHILE STERILISING.

A level and cold surface must now be prepared upon which the glass slips may rest in pouring out the gelatine over them. A levelling tripod is employed with this view, on which is placed a flat glass dish filled with ice and water, and covered by a sheet of window or plate glass, care being taken to exclude all air.

When the sheet of glass is sufficiently cold, a sterile slip is taken out of the iron box, and having been quickly turned with the lower surface upwards, is laid on it and covered with a bell-jar. The gelatine is then poured in a uniformly thin film over the slip, but in such a manner that it does not run over the edge. In a few minutes it will solidify, and when this has happened the slip is transferred, as rapidly as possible, to a moist chamber constructed in the following manner:—

FIG. 41.—ICE APPARATUS FOR MAKING GELATINE PLATES.

Moist Chamber.—A flat-bottomed glass dish is inverted over another smaller in size. The bottom of the latter is covered with a piece of bibulous paper soaked in corrosive sublimate

FIG. 42.—MOIST CHAMBERS.

solution (1 to 1000). The interior of the chamber is also rinsed out with sublimate, and the excess allowed to escape.

The glass slips covered with the gelatine are placed in the chamber the one over the other, but separated by small glass benches on which they rest.

Glass Troughs.—In order to prevent the gelatine running over the glass slip the latter is sometimes provided with a raised margin so as to convert it into a shallow trough. Besides preventing the gelatine from running over, these troughs aid in making the gelatine film of uniform depth.

73. **Esmarch's Modification of Above** (No. 366, i. 1886, p. 293). The tubes are inoculated as in the foregoing, but instead of the contents being poured out on plates, the tube, with the melted gelatine in it, is rotated in iced water, or under a water tap, so as to spread it equally over the interior. The organisms grow in the film of jelly, and can be examined from time to time under the microscope, through the wall of the tube. The cotton plug should be cut short and singed, and a caoutchouc cap slipped over the end of the tube, before immersing in the water. A small simple lens is manufactured by Rohrbeck which can be attached to the tube and which is useful in counting the colonies.

The method is particularly serviceable in **testing water** for germ impurities, as

it does away with the fallacy of including in the reckoning any atmospheric germs which may have accidentally fallen on the plates in the ordinary Koch's procedure.

FIG. 43.—ESMARCH'S APPARATUS FOR COUNTING COLONIES IN A TUBE.

Arloing (No. 4, x. 1887, p. 276) recommends the use of long flat tubes instead of those which are cylindrical. The gelatine is run out on one side only, and in a more uniform film, so that the counting of the colonies is rendered less difficult. The organismal growths can also be examined microscopically with greater ease.

74. **Appearance of the Cultures.**—In from a few hours up to two or three days, the organisms begin to grow in separate colonies. The slips may, from time to time, be carefully removed from the moist chamber and examined on the stage of a microscope. The examination of the colonies with a low power of the microscope, at an early period of their growth forms an important means of diagnosis.

FIG. 44.—WOLFFHÜGEL'S APPARATUS FOR COUNTING COLONIES ON A PLATE CULTURE.

The fact of one organism liquefying the medium while another does not, or of one being coloured, another uncoloured, is of great diagnostic value. The border and surface of the colony, the rapidity of growth, etc., are all features by which they may be distinguished.

Apparatus for Counting Colonies.—This usually consists of a plate of glass divided into centimètre squares by a series of ruled lines. Certain of the squares in Woffhügel's apparatus are further subdivided. It is set in a frame, and when about to be used is placed over the gelatine plate. The smallest and the largest number of colonies in some of the squares are counted with the aid of a lens, and an average is struck.

Method of Inoculating a Tube.

75. Granted that a plate culture has been successful and that several distinct colonies have shown themselves in the plate of last attenuation, the next thing to be done is to inoculate separate tubes from each colony by means of a thin platinum wire set in a glass rod. It is sometimes advantageous to use a needle with a loop upon the end (Ger., öse), as where a drop of liquid has to be transferred from one tube to another or where the gelatine surface has to be scratched or indented. The wire for this purpose ought to be a little thicker than in the former case.

The straight wire or the öse, as the case may be, is heated to redness in a Bunsen flame. When cool, the colony is touched with its point so as to remove a very small quantity of the growth. If the inoculation is to be made from one tube to another the tube containing the culture is held with its mouth downwards, or nearly horizontal if the medium be liquid. The plug is withdrawn with as little disturbance as possible; and the wire is insinuated into the tube without touching its walls. The same precautions are taken in opening the tube into which the culture is to be introduced. The needle is plunged into the centre of the gelatine mass, and is pushed down close to the bottom of the tube; or if a surface culture is desired, the öse is drawn along the flat surface from end to end, and made to pierce the gelatine at intervals in its course. In both cases the track of the needle should be as narrow as possible. When the inoculation is completed, the plug is replaced, and a label is at once attached to the tube indicating the nature of the culture, the date, and such other particulars as may be thought necessary. It is a great saving of trouble to have blank labels ready pasted on all tubes ready to fill up as required. The tubes when inoculated should be kept in a stand where the progress of the culture can be readily observed.

Fig. 45.—Stand for holding Inoculated Culture Tubes.

As regards the **recognition** of particular disease and other germs the reader is referred for details to the Chapters on *Vegetable Parasites* (vol. ii.)

The Incubation Chamber.

76. Temperature exerts a most fundamental influence upon the rapidity and luxuriance of the growth of various organisms.

Some organisms begin to germinate at a lower temperature than others. According to Flügge (No. 359, p. 528) many **saprophytes** show the first signs of multiplication at 6° C., **cholera spirillum** at from 15° to 16°, **tubercle bacillus** at 33°, **lactic acid bacilli** at 43·5°, **bacterium termo** at from 40° to 43°, and **bacillus subtilus**, at from 50° to 55°. The highest limit is difficult to determine.

The bacteriologist must, accordingly, provide himself with one or more incubators in which cultures may be retained at any desired temperature. An incubator consists of a double-walled chamber, with water interposed between the walls, whose temperature is kept constant through a gas flame regulated by a thermostat. The door may be made of glass, but this is practically of little advantage. It should be provided with a number of movable shelves. A small Bunsen or Koch's automatic safety burner furnishes the best flame.

FIG. 46.—ROHRBECK'S CULTURE CHAMBER, WITH GLASS DOOR, THERMO-REGULATOR, AND TWO THERMOMETERS, ONE FOR THE WATER, ANOTHER FOR THE CHAMBER. COVERED WITH FELT.

The whole apparatus should be covered with felt, and the roof must have an aperture for the insertion of a thermometer. In some incubators a small dish containing water is placed on the floor

for the purpose of keeping the atmosphere moist. A hygrometer is usually inserted, when this is so, through a second perforation of the roof.

Communicating with the water chamber is another perforation in the roof into which the thermostat can be inserted. The thermostat may even with advantage be placed in a small side chamber fastened on to the incubator.

FIG. 47.—KOCH'S AUTOMATIC SAFETY BURNER. DOUBLE.

THE THERMO-REGULATOR.

77. The most of those in general use depend for their action upon the expansion of ether and mercury by heat. The accompanying scheme (Fig. 48) will serve to illustrate the principle on which they are constructed:—*v, v, v,* is an outer glass tube with a bulbous lower extremity and with a neck into which fits a perforated cork (*c*). The bulb is partially divided into two compartments by the partition *t*, a free communicatian, however, existing between the outer and inner compartments below, while they are separate above. The lower part of the bulb is filled with mercury (M.), the upper (E.A.) with a mixture of equal parts of ether and alcohol (v. Meyer). An exit tube (*ext.*) is attached to the stem. Through the perforation in the cork a slender tube (*p*) is inserted. The lower end is bevelled off, while a short way above the bevelled extremity is a minute pin-point aperture (*a*). The entrance tube (*ent.*) is connected with the gas supply, the exit tube (*ext.*) with the Bunsen burner. The Bunsen should be so constructed that it will burn with the smallest possible supply of gas, and also afford a larger flame when required. The space underneath the incubator in which it is placed should be surrounded with metal to

avoid currents of air and as a security against accident from fire. It is well also to have the whole apparatus set upon a stone or concrete slab.

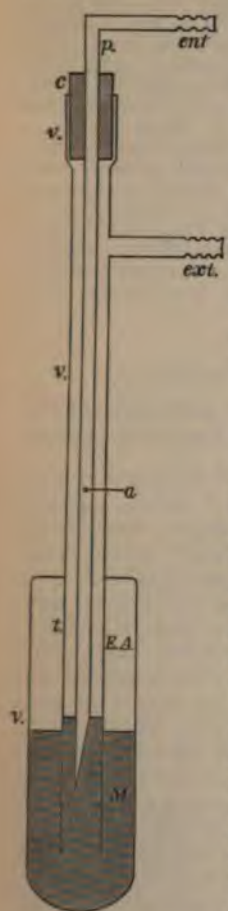

FIG. 48.—DIAGRAMMATIC SCHEME OF A THERMO-REGULATOR: *ent.*, entrance tube; *ext.*, exit tube; *v*, outer tube; *p*, inner tube bevelled off at its end; *t*, partition; E.A. ether and alcohol mixture; M., mercury; *c*, cork.

When the temperature has reached the desired height, the inner tube (*p*) of the thermo-regulator is pushed down until the bevelled extremity sinks underneath the mercury. The supply of gas will then be derived exclusively from the pin-point aperture (*a*), and the flame will consequently be reduced to a minimum. If the temperature sinks, the ether and mercury contract and allow gas again to escape from the end of the tube.

FIG. 49.—ROHRBECK'S THERMO-REGULATOR.

To construct a good thermo-regulator two points ought to be attended to. Firstly, mercury ought not to be employed alone, but the upper part of the bulb ought to be filled with alcohol and ether; and, secondly, the extremity of the tube should be so finely bevelled that a sudden gush of gas is prevented when the mercury sinks. In order to avoid this it is almost better to have simply a narrow slit of uniform size in the end of the tube.

To prevent disturbance of the apparatus from alterations in the pressure of the gas-supply a Moitessier's gas regulator may be interposed between the gas connection and the thermo-regulator. Simpler instruments than that of Moitessier are furnished by most gas companies, which may be attached to the main supplying a whole laboratory. It will be found, however, that if the stopcock at the gas connection is simply turned half down there is little occasion for either of these. The expansion of the ether on the slightest increase of temperature is so great that it almost instantaneously drives up the mercury and reduces the size of the flame. Among the best thermo-regulators are those of Bunsen-Meyer, Rohrbeck, Reichert, and Page.

Other systems of regulating the size of the flame have been recommended, but none are so satisfactory as the mercury instrument supplemented with ether.

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Filtering the Organisms from a Liquid.

78. This can be done by passing the liquid through many folds of filtering paper, but paper is never so reliable as faience porcelain or gypsum.

Miquel and Benoist (No. 354, xxxv. 1881, p. 552), employ the following simple and ingenious apparatus. A flask (A) is made with a long wide neck, into which a funnel with an air-tight plug can be inserted. From the bulb of the flask a small tube (*p*) comes off, ending in a capillary extremity. The lower part of the neck of the flask (*a*) is filled with asbestos, while into the upper part, for about two-thirds of its height, a mixture of 46 parts water, 52·4 parts plaster of Paris, and 1·6 parts asbestos is poured and allowed to solidify. The flask so prepared is dried in a hot chamber for one to two weeks at a temperature of 60° C. The point of the tube *p* is next closed in a flame, and the apparatus is slowly heated to a temperature of 170° to 180° so as to sterilise it. When about to be used a little water is poured over the plaster, in order to fill the pores and cause it to adhere closer to the neck of the flask. The neck of the tube *p* is broken under distilled water. The flask is gently heated and again allowed to cool, whereby some water is aspirated into it. The water is now boiled, and after sufficient has been thus removed, the tip of the tube *p* is again closed and the funnel filled with the liquid to be filtered. As the flask cools the steam condenses and leaves the vapour within under abundantly negative pressure. The liquid in the funnel containing the germ impurity is thus powerfully aspirated through the plaster medium and purified.

Fig. 30.—Miquel and Benoist Apparatus for Filtering Liquids containing Bacteria.

A more elaborate filter, in which porcelain is used, is that of Chamberland. For detailed description consult No. 94, August 4, 1884, and of February 21, 1885; or No. 363, p. 21.

STAINING OF BACTERIA.

79. All bacteria are more or less coloured by means of basic aniline dyes (Sect. 43). As a rule they take on a deep colour almost instantaneously, and retain it in presence of decolorising reagents in preference to the histological elements of the part.

Two views are held explanatory of this property. The one is that the stains construct **chemical compounds** with the bacteria; the other is that they simply **dialyse** with unusual ease into their interior.

The capsules of bacilli are much more permeable in some instances than in others. Young bacilli stain more readily than old, but are sooner deprived of their colour by nitric acid or by other decolorising reagents.

MORDANTS.

80. Certain substances, when added to these basic aniline dyes, have the property of fixing them on the bacteria, so that they become more insensitive to the action of decolorants.

How they act is not definitely known. It is possible, on the one hand, that aniline, or other such mordant, acts by rendering the bacillus more accessible to the colouring matter, and, on the other, that a new substance is formed by the combination of the dye and the mordant which then penetrates the bacillus.

The mordants in general use are chiefly **aniline oil, benzaldehyd, salicylic aldehyd, vanillin** (Ehrlich), **turpentine** (Prior), **toluidin** (Fraenkel), **carbolic acid** (Ziehl and Neelsen), **ammonia** (Weigert), **borax** (Sahli), etc. Aniline oil and carbolic acid are two of the most serviceable. They not only fix the dye upon the organism, but render the coloration more brilliant.

ORDINARY STAINING SOLUTION FOR BACTERIA IN A TISSUE.

81. A quantity of commercial aniline oil, sufficient to make a saturated solution, is shaken up with distilled water and allowed to stand for a few minutes. When the water is saturated with the aniline, it is filtered, and 100 c.c. are mixed with 11 c.c. saturated alcoholic solution of fuchsin, methyl-violet, or some other basic aniline dye.

This mixture can be employed for any vegetable micro-parasite **in a tissue**. It is not so suitable for cover-glass preparations unless when subsequently washed out with nitric acid, as it is apt to leave a deposit. That made with fuchsin is specially adapted for colouring the tubercle bacillus. As the solution decomposes in a few days, the two ingredients should be mixed always just before use.

If the organism has been **dried on a cover-slip** (Sect. 88) it is better to employ simply a $\frac{1}{4}$ per cent watery solution of gentian-violet or fuchsin, or a saturated watery solution of methylene blue. In the case of the gentian-violet or fuchsin the solution is dropped on to the cover, and after remaining in contact for a half to three-

quarters of a minute, it is rapidly washed off in water, dried, and mounted in solution of gum-dammar or Canada balsam in xylol. With the methylene blue, it is better to swim the cover on the surface in a watch-glass, and to leave it in contact for four or five minutes.

GRAM'S PROCESS.

82. This is also specially suitable for organisms contained in sections of tissues. The tissue should have been hardened in alcohol.

The staining fluid consists of a basic aniline dye, such as gentian-violet or fuchsin combined with aniline water. Commercial aniline oil is mixed with distilled water in the proportion of 5 parts to 100. The mixture is well shaken and is filtered. To 100 parts of the filtrate 5 parts of a saturated solution in alcohol of either of the above dyes is added, and the two are vigorously mixed.

The sections are left in this for nine minutes, and are next washed in water and placed in a solution of iodine with potassic iodide of the following strength :—

Potassic iodide	1 grm.
Water	20 c.c.

Metallic iodine, as much as will dissolve.
Dilute with three times the quantity of water.

The sections should be left in the iodine until they become dark-brown coloured. They are next washed in alcohol (methylated spirit) until they have become almost entirely decolorised, only a faint yellow tint remaining.

The organisms should have a deep blue colour, while their surroundings are colourless. If the colour is still found to be too deep, place the section again in the iodine, and repeat the washing in alcohol.

Bismarck brown or hæmatoxylene may be employed as contrast stains. The preparations are clarified in oil of cloves or in cedar oil.

DOUBLE STAINING OF BACTERIA.

83. Several methods may be adopted so as to stain the spores of one colour, the rods of another. Berlioz (quoted by Cornil and Babes, No. 302, p. 67) recommends the following procedure :—

1. Make a solution of 6 c.c. aniline oil in 84 c.c. distilled water. Dissolve by heat and filter when cool. Add 2·5 grm. methyl-violet (6 B superfine of Bale) dissolved in 10 c.c. alcohol at 90° C. and filter.

2. Make a solution of 2·5 grm. coccinine, 9·5 c.c. distilled water, 5 c.c. alcohol at 90° C. Dissolve and filter.

Mix equal parts of the two solutions.

Leave the sections in the staining fluid for quarter of an hour or more. Treat with a 5 per cent solution of carbonate of soda or iodide of potassium. Wash in water and mount in balsam in the usual way, employing clove oil as the clarifying agent.

Coccinine gives a beautiful red and possesses all the advantages of eosin as a ground stain where the bacilli or micrococci are coloured blue or violet. It also demonstrates the nuclei of the tissue. It may be employed in strong or in weak solution. It can be used as a contrast stain for tubercle bacilli after the preparation has been decolorised with nitric acid.

Flügge (No. 359, p. 643) draws attention to the fact that if the cover-glass on which sporing bacilli have been dried be drawn six times through the flame instead of the usual three times, or be kept at a temperature of 180° to 200° C. for quarter to half an hour, the spores take on the dye much more readily. He employs the ordinary aniline fuchsine used for tubercle bacillus (Sect. 84); and the further procedure is exactly like that for this bacillus.

DIFFERENTIAL STAINING OF TUBERCLE BACILLI.

84. The principle involved in all the numerous procedures recommended for staining tubercle bacilli is alike. It is founded upon the fact that if they are deeply coloured with a **basic aniline dye,** especially one to which some **mordant,** such as any of those previously mentioned (Sect. 80) has been added, they retain the colour in presence of certain reagents which decolorise the surrounding tissues. The usual decolorising agents employed are **vesuvin, nitric acid, alcohol,** etc.

Syphilis bacilli have, according to Bienstock (No. 11, iv. 1886, p. 193) the same property, and he is of opinion that the cause is to be found in the bacilli being surrounded by a layer of **fat.** The fat stains readily with most basic aniline dyes. He found (*loc. cit.*) that various bacilli cultivated on agar-agar to which 20 per cent fat had been added, can be made to stain differentially like those of tubercle. Gottstein (No. 11, iv. 1886, p. 193) arrived at a similar result.

(*a*) **Koch's original method** (No. 44, ii. 1884, p. 5).—1 c.c. of a saturated solution of methylene blue is shaken up with 200 c.c. distilled water, and to this 0·2 c.c. of a 10 per cent solution of potash are added, and the whole again shaken. Cover-glass preparations of sections of tissues containing the bacillus are left in this for twenty-four hours. They are afterwards placed in a saturated solution of vesuvin, which destroys the blue colour in all parts, unless in the bacilli, while it imparts to the surrounding tissues its own brown colour. The bacilli are then seen stained of a blue colour on a brown background. The preparations are clarified in cedar oil or turpentine. They may, further, be washed in xylol and mounted in Canada balsam or gum dammar dissolved in xylol or turpentine.

(*b*) **Ehrlich-Weigert Method** (see illustration, Pl. V., Fig. 86). This method is said by Koch (No. 44, ii. 1884, p. 6) to be even preferable to his own.

A. Make a saturated solution of some basic aniline dye, such as fuchsin or gentian-violet, in absolute alcohol.

B. Make a saturated solution of commercial aniline oil in distilled water, by shaking up an excess of the former with the water and filtering.

Add 11 c.c. of A to 100 c.c. of B and filter.

Stain the tissue or cover-glass for from five minutes to twenty-four hours in it. If it is warmed until vapour begins to be given off, the bacillus stains more rapidly (Rindfleisch).

Decolorise in 1 part nitric acid to 2 parts distilled water. Wash thoroughly in water. It will be found that some of the colour returns. If too deep, place again in the acid.

Where fuchsin is employed, the best contrast stain is saturated, watery solution of methylene blue. Leave the section or cover-glass in it until it assumes a deep blue colour (five minutes). Pass through spirit and oil of cloves, and wash with xylol. Mount in solution of Canada balsam or gum dammar in xylol.

When the preparation is placed in the nitric acid it assumes a brown colour. Ehrlich says this is due to a triacid combination, and that the return of the colour when transferred to water is owing to this being converted into a monacid compound.

Where nitric acid cannot be employed as a decolorising reagent, as in the case of some delicate tissues, Ehrlich recommends:—

(1) Staining in watery solution of fuchsin for twenty-four hours.

(2) Staining in fuchsin-aniline solution for twenty-four hours.

(3) Washing with alcohol and subsequent treatment with a mixture of one part nitric acid to two parts saturated solution of aniline sulphate followed by careful washing in water.

(4) Steeping in saturated solution of bisulphite of soda for twenty-four to thirty-six hours.

(5) Laying the tissue in water which has been boiling a short time previously.

The remaining technique as in the ordinary method, but without contrast staining.

He says the procedure is particularly useful for detecting tubercle bacilli which cannot be demonstrated by other means.

(*c*) **Ziehl-Neelsen Method.**—Carbolic acid is employed as the mordant instead of aniline oil. The stain is faster than in the case of the Ehrlich-Weigert dye. Neelsen's process (No. 11, iii. 1885, p. 200), which is a modification of that proposed by Ziehl (No. 93, 1882, No. xxxiii. and 1883, No. xvii.) is the following:—

Fuchsin	1 grm.
Carbolic acid . . .	5 c.c.
Alcohol	10 ,,
Distilled water . . .	100 ,,

The solution ought to be heated in order to stain cover-glass preparations rapidly. At an ordinary summer temperature, sections of tissues stain in from five to ten minutes. They are decolorised in 25 per cent sulphuric acid in water, and are afterwards stained in methylene blue. The solution can be kept for many weeks without undergoing decomposition.

The resulting stain is perhaps more brilliant and more permanent than that obtained by any other method.

(*d*) **Fütterer's Method** (No. 13, ci. 1885, p. 198) is essentially a modification of Ehrlich's process for staining tubercle bacilli in tissues.

(1) Stain by Ehrlich's method.

(2) Wash out in alcohol to which a small quantity of dilute nitric acid has been added (two to three drops in a watch-glass) until a light rosy colour has been obtained.

(3) Lay the section for a minute in a well-filtered solution of chloride of palladium (1 to 500).

(4) Wash in water.

(5) Place for a few minutes in acidulated alcohol.

(6) Transfer to cedar oil.

(7) Mount in Canada balsam dissolved in turpentine.

The advantages are that the staining of the bacilli is darker than by the ordinary method, and it is less susceptible to the decolorising action of chloroform, ether, alcohol, etc.

(*e*) **Gibbes' Method.**—It is applicable for staining the bacillus either in sputum or in a tissue. The receipt for the staining solution is the following (No. 15, 1885, p. 173):—

A.	Rosaniline hydrochloride . .	3 grm.
	Methyl blue	1 „

Rub these together in a mortar.

B.	Aniline oil	5 c.c.
	Rectified spirit	20 „

Dissolve and pour B drop by drop into A, stirring vigorously. Then add 20 c.c. distilled water and keep in a stopper bottle. When it is employed for sputum make a cover-glass preparation, as afterwards described (Sect. 88). Warm the staining solution, float the cover-glass on it for four to five minutes, and wash in spirit until any colour ceases to be given off. Dry and mount in xylol balsam. If the solution is not heated, half an hour should be allowed for the staining. Sections of tissues may be stained by immersing them in the warm solution for from five minutes to half an hour, and washing out in spirit as before. The bacillus stains red, and other bacteria and the background blue. The staining liquid is liable to decompose.

STAINING OF SYPHILITIC BACILLUS.

85. Lustgarten (No. 46, i. 1885) states that the following is the only procedure by which he has been able to accomplish it:—

The sections are to be placed for twelve to twenty-four hours in a mixture of 11 parts saturated alcoholic solution of gentian violet in 100 parts watery solution of aniline oil at an ordinary temperature, and afterwards for about two hours at a temperature of 60°. They are next transferred for a few minutes to absolute alcohol, and

for ten seconds to a $1\frac{1}{2}$ per cent solution of permanganate of potash, after which they are immersed in strong sulphuric acid until the colour disappears. If after the first immersion it has not entirely vanished the procedure is repeated. The preparation is subsequently washed in water, dehydrated, clarified with oil of cloves, and mounted in balsam.

STAINING OF THE PNEUMOCOCCUS.

86. Friedländer (No. 11, iii. 1885, p. 757) adopted the following method of showing the capsule of the coccus of acute pneumonia. A cover-glass preparation is made (Sect. 88), and is drawn three times through the flame. The cover is next placed for a few minutes in a 1 per cent acetic acid solution. The superfluous acetic acid is then blown off by a pointed tube, and the preparation quickly dried in the air. It is next placed in saturated aniline-water gentian-violet solution for a few seconds, washed in water, and examined. The acetic acid removes a substance which is readily stained by the gentian-violet, thus leaving in the preparation when finished a pale background on which the brightly stained capsules are readily detected.

When the cocci are lying in a tissue, he recommends staining them for twenty-four hours in acid gentian-violet (saturated solution of gentian-violet in alcohol fifty, distilled water one hundred, and acetic acid ten), decolorising in 1 per cent acetic acid for one or two minutes, clarifying by alcohol, oil of cloves, etc.

STAINING OF TYPHOID BACILLUS.

87. Gaffky (No. 44, ii. 1884, p. 378) recommends the following procedure :—The organ is hardened in alcohol, and the sections from it are left in a deep blue fluid made by pouring saturated solution of methylene blue in alcohol into distilled water. The fluid ought to be prepared fresh each time it is used. They are afterwards washed in distilled water, clarified in alcohol and turpentine, and mounted in Canada balsam.

STAINING OF ACTINOMYCES.

88. (1) Weigert (No. 13, lxxxiv. 1881, p. 285) first recommended staining actinomyces with archil (orseille). It has a special affinity for them. Ordinary archil, however, is seldom pure, and consequently stains some of the surrounding tissues as well. Israel (No. 13, cv. 1886, p. 169) employs orcëin,[1] which is said to be a chemically pure substance ($C_4H_7NO_6$). A saturated solution should be made so as to overstain the preparation. The latter is washed down to the necessary

[1] The particular orcëin he uses is obtained from the manufactory of Dr. Theodor Schuchardt of Görlitz.

colour with alcohol, care being taken not to wash out too much. It stains the organism of a Bordeaux-red colour.

(2) An excellent method will be found to be the following:—Stain the sections in Ziehl-Neelsen's solution of fuchsin (Sect. 84). Wash in water, and then decolorise in saturated alcoholic solution of picric acid. When the red colour has almost entirely left the section, place the latter in a large vessel of water and leave it there for twenty-four hours, the water being frequently changed. Pass it through spirit, oil of cloves, and xylol, and finally mount in gum dammar dissolved in xylol. The actinomyces stain deep red on a yellow background.

PREPARATION OF TISSUES AND LIQUIDS CONTAINING ORGANISMS FOR STAINING.

When Lying in a Tissue.—Harden in alcohol, soak in "A" or "B" freezing fluid after removal of the alcohol by water, and cut in the freezing microtome. If the tissue is very delicate or porous, as in the case of the lung, it may be embedded in celloidin.

A cover-slip preparation of the organisms in a tissue may be made by gently rubbing a small fragment of tissue while fresh over the cover-slip and drying. Some of the organisms will be found to adhere.

When contained in a Liquid.—Place a fraction of a drop of distilled water on a cover-slip, mix a little of the liquid with it, as uniformly as possible, and keep rubbing and mixing with an öse until quite dry. Pass the cover three times over the flame of a Bunsen lamp immediately before staining.

For further particulars see Sect. 81.

Phthisical Sputum.—It should be treated very much as when contained in an ordinary liquid. The tubercle bacillus is sometimes uniformly scattered through the sputum. More often, however, it is concentrated in the little cheesy masses detached from a cavity. These should, accordingly, be sought for and rubbed over the cover-slip.

Methods of Staining Bacteria.—**Babes:** Arch. f. path. Anat., cv. 1886, p. 511. **Bermann** (Method of Staining Tubercle Bacillus): Med. News, Phila., xliii. 1883, p. 593. **Bujwid** (Chemical Reaction of Cholera Bacilli): Zeitschr. f. Hygiene, ii. 1887, p. 52. **Burrill** (Method of Staining Tubercle Bacillus): N. Y. Med. Rec., xxiv. 1883, p. 651. **Cheyne** (Methods for Bacteria): Brit. Med. J., 1884, ii. p. 487; Practitioner, xxx. 1883, p. 241. **Gibbes:** Brit. Med. J., 1882, ii. p. 735. **Gottstein** (Influence of Fat on Staining): Fortschr. d. Med., iv. 1886, p. 252. **Gram** (Staining of Schizomycetes): Fortschr. d. Med., ii. 1884, p. 185. **Günther** (Staining of Recurrens Spirilla in Blood): Fortschr. d. Med., iii. 1885, p. 755. **Friedländer** (Staining of Capsule Coccus): Fortschr. d. Med., iii. 1885, p. 757. **Petri** (Staining of Tubercle Bacillus): Berl. klin. Wochnschr., xx. 1883, p. 739. **Vignal** (Tubercle Bacillus): Compt. rend. Soc. de Biol., iv. 1883, p. 343. **Weigert:** Arch. f. path. Anat., lxxxiv. 1881, p. 275.

INOCULATION OF ANIMALS.

89. The mouse, rabbit, and guinea-pig are all suitable for the purpose. The inoculation in some cases (anthrax) can be made on a

mere scratch of the skin, the ear, more especially in rabbits, being a convenient site. If the medium of inoculation be solid (tubercle) a

FIG. 51.—KOCH'S SUBCUTANEOUS INJECTION SYRINGE.

little pocket of skin may be made at the root of the tail, and a portion of the virus inserted within it on an öse. In other cases it may be necessary to introduce the virus by means of a sterile finely-pointed syringe.

CHAPTER IX

PRACTICAL BACTERIOLOGY—(*Continued*)

Attenuation of Pathogenic Microbes.

90. The fact that a disease microbe can exist in different states of virulency, and that when so attenuated may still act as a vaccine, was first demonstrated by Pasteur on the micro-organism of fowl cholera. Since then, several other pathogenic microbes have been the subject of experiment, more especially anthrax, both at Pasteur's and at other hands. The result has been to show that the virulent properties of these bodies may be modified by various means other than that devised by Pasteur and still retain their power of conferring immunity from a future attack of the disease.

PASTEUR'S ORIGINAL METHOD.

91. In a note to the French Academy of Medicine, published in the *Bulletin de l'Acad. de Méd.* of Oct. 26, 1880,[1] Pasteur described how the virus of **fowl cholera** can be attenuated by long exposure to air. The most virulent form of poison, that taken from an animal just dead of the chronic variety of disease, is cultivated on **chicken bouillon** for three, four, five, or eight months or more. By this time the virus becomes so diluted that perhaps only one in ten animals dies after being inoculated. A stage is at length reached in which the virus does not kill, but nevertheless acts as a vaccine. When the flasks containing the culture are sealed up with a limited amount of air, it is found that time does not have the same attenuating influence as when the culture is freely exposed to atmospheric oxygen. Pasteur, therefore, regarded the cause of the attenuation as being the prolonged **contact with oxygen.**

He afterwards found that **anthrax** similarly cultivated at a temperature between 42° and 43° C. daily loses part of its virulence, until, by the ninth day, it becomes inert. The inoculation of sheep with

[1] See also No. 40, xci. 1880, p. 673.

attenuated anthrax, he asserted, nevertheless secures them against the attacks of the organism in its full virulence, that is to say, it acts as a **true vaccine.** Fresh cultivations can be made at different stages of attenuation and be retained in these states.

He supposed that here, as in the case of the fowl cholera, the **atmospheric oxygen** was the attenuating agent.

About the time that Pasteur was conducting his researches in France, Greenfield (No. 362, xvi. pt. i. Ap. 1880; and *Ibid.*, xvii. pt. i.; *also*, No. 149, June 17, 1880; *also*, No. 59, Dec. 18, 1880, and Jan. 1, 1881; *also*, No. 6, Dec. and Jan. 1880-81), in this country, employing the same method of attenuation for **anthrax** as that used by Pasteur for **fowl cholera,** discovered that anthrax taken from the guinea-pig was so modified in its action by repeated cultivation as to become, in course of time, totally inert, and that each successive generation was feebler than that preceding it.

Koch, Gaffky, and Loeffler (No. 44, 1884, ii. p. 147) repeated Pasteur's experiments with his own vaccine, and with anthrax attenuated by themselves. They found that anthrax attenuated at 42·6° C. is still sufficiently strong to kill **mice** after twenty days cultivation (mouse anthrax), but had little effect upon **guinea-pigs** and **sheep.** After twelve days culture it will still kill guinea-pigs but not sheep. It proves fatal to sheep up to six days of cultivation. They were thus able to procure anthrax with different physiological intensities, although the bacilli presented the sharply-cut extremities, and elongated into threads containing spores as in the normal condition of the parasite.

They, however, regarded the **temperature** at which it is cultivated as the attenuating agent, not the contact with oxygen as Pasteur had supposed. They found, for instance, that between the upper and lower parts of the incubator they used, there was a difference of almost a degree, and that this was sufficient to occasion the greatest uncertainty in the attenuation of different flasks placed within it.

They were successful, as Pasteur had been, in rendering sheep insensitive in most cases to the effects of the organism, but found that the procedure did not succeed in every case (p. 165) when a very strong anthrax was reinoculated.

92. **Pasteur's system of inoculation** for anthrax, as practised in France at the present day, consists in employing two strengths of attenuated virus (*le premier* and *le deuxième vaccin*). The former will not kill rabbits or guinea-pigs, but is fatal to mice, and is obtained by cultivating for fifteen to twenty days at a temperature between 42° and 43° C. The latter is obtained after cultivating for ten to twelve days. It is consequently more powerful. An interval of from twelve to fifteen days is allowed to elapse between the two inoculations.

The adoption of this means of protecting animals from the ravages of anthrax is said to have been attended, in France and elsewhere, by an enormous decrease in the mortality from this disease. Whether it is a means of protecting the animal in all cases, and for all time,

against anthrax may be disputed, and is denied by many. It very likely does not do so in all instances, no more than an attack of small-pox confers a perfect immunity from a future attack. If, however, it renders sheep and other domestic animals *less liable* to be again attacked, and if when attacked they take the disease in a *milder form*, a very great object has been gained. This, so far as one can judge, has been accomplished.[1]

SANDERSON'S METHOD.

93. Another expedient for furnishing a vaccine against anthrax was suggested by Sanderson and carried to experimental proof by Duguid (No. 362, xvi. 1880, pt. 1, p. 267). It was based on the fact that anthrax loses much of its virulence when passed through the system of a rodent (guinea-pig), so that when introduced into that of an ox it might be supposed to communicate the disease in a mild form, but yet ensure against a future attack.

Greenfield (No. 362, xvi. 1880, pt. 1, p. 273) found that the blood of the guinea-pig affected with anthrax, inoculated into the ox, induces anthrax fever, but almost always without a lethal result.

Pasteur and Thuillier's researches on **rouget des pores** point to the fact (No. 40, xcvii. 1883, p. 1169) that when the microbe of this disease is inoculated on a series of pigeons, it progressively becomes more virulent for the pig, but when passed through the systems of a series of rabbits, there arrives a time when the poison reproduces the disease in pigs in a very mild form, but renders them proof against the undiluted poison.

Pourquier (No. 40, ci. 1885, p. 863; *Ibid.*, civ. 1887, p. 703) asserts that **sheep-pox virus** can be attenuated by inoculating it on subjects having had variola, or which have been vaccinated at a former period (at least three years).

ATTENUATION BY HEAT.

94. Toussaint (No. 40, xci. 1880, p. 135; *Ibid.*, note p. 303) made the discovery that anthrax, when rapidly heated up to a certain temperature, loses much of its virulence and can be utilised as a vaccine.

Chauveau (No. 40, xciv. 1882, p. 1694) took up the subject and showed what the range of temperature is at which this attenuation takes place. It is pretty wide, and can be modified according to the

[1] Pasteur's first experiments on a large scale were carried out in the year 1881 at Pouilly-le-Fort. In a recent letter to the author on the subject of the efficacy of his method of vaccination, he writes:—

"Double vaccination is always employed. It confers a complete immunity. The Society of Agriculture of Melun, which previously made the famous experiment at Pouilly-le-Fort, has quite recently repeated it. Twenty sheep were divided into lots of ten each. The sheep in one of these lots were inoculated with the double vaccine. The whole twenty sheep were afterwards inoculated with virulent anthrax. The vaccinated lot resisted completely, while, of the unvaccinated, seven died, and the three others turned very ill.

"The immunity conferred by the double vaccination does not last indefinitely, but sufficiently long for practical purposes, and for the usages of commerce."

time the virus is exposed. The following are particulars of his methods :—

Chauveau's First Observations.—The blood of a guinea-pig inoculated with virulent anthrax for thirty-six to forty-eight hours is received in small pipettes. After it has coagulated, the clot is broken up so as to allow the serum to exude, and the ends of the pipettes containing the blood are inserted in water heated to the necessary temperature. The blood must not be exposed in large mass, otherwise it becomes unequally heated.

An exposure of the blood for nine to ten minutes at +55° C. suffices to kill the bacilli, but if it is exposed for eight, seven, six, or five minutes, the bacilli may be retained living and deprived of their virulence. This, however, is never so certain a procedure as when a lower temperature is employed.

At a temperature of +52° C. an exposure of fifteen to sixteen minutes will destroy their vitality. By an exposure for fourteen minutes it retains its vitality, and an extremely attenuated vaccine is obtained. The less the time of exposure, the less is the corresponding attenuation.

With a temperature of +50° C. it requires twenty minutes to destroy the vitality of the bacillus. The best of all vaccines is obtained by employing this temperature for eighteen minutes. An exposure for ten minutes renders the attenuation evident, but is not sufficient to ensure the employment of the vaccine with safety.

A first inoculation with a weak vaccine (blood heated to +50° for fifteen minutes), and a second inoculation after an interval of from ten to fifteen days with a stronger vaccine (blood heated for eight to ten minutes), preserve sheep from the effects of the most powerful virus.

The attenuation of the virus is accompanied by a corresponding diminution in the rapidity of the proliferation of the bacillus.

He holds that virus attenuated by this means is as effective a vaccine as that prepared by Pasteur's method.

For the attenuation of anthrax spores a much higher temperature is necessary (+80° C.).[1]

Chauveau's Later Method.—The method he adopted later on for the attenuation of anthrax, as summarised in a communication to the Academy of Sciences (No. 40, xcvii. 1883, p. 1397) is briefly as follows. Two liquids are used.

Preparation of Liquid No. 1.—(1) Inoculate chicken broth with a drop of fresh anthrax blood ; (2) Cultivate the virus as a fragmented mycelium devoid of spores at a constant temperature of +43° C. ; (3) Heat the culture for three hours at a temperature of 47° C. to attenuate the mycelium. A number of other cultures are then made from it which are utilised for preventive inoculation purposes.

Preparation of Liquid No. 2.—(1) inoculate fresh broth with one or two drops of the above attenuated culture ; (2) cultivate this for five to seven days at a temperature of 35° to 37° C. in order to develop a mycelium and spores already attenuated ; (3) heat at 80° C. for one hour to complete the attenuation.

Both of these liquids are utilised in the inoculation of sheep (No. 40, xcvii. 1883, p. 1242). He employs them for a double vaccination in the same manner as Pasteur does his *premier* and *deuxième vaccin* (see p. 142). That which is attenuated at 80° is used as the *premier vaccin*, and that which is attenuated at a lower temperature as the *deuxième*.

The success attending the procedure, he says, has been so complete as to render sheep completely refractory to repeated inoculations of the most virulent anthrax.

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[1] See No. 40, xcvi., Seance of 26th February, 5th and 12th March, and of 21st May 1883.

It should be noted that the virus attenuated at a low temperature apparently takes longer to regain its virulent properties than one which has been attenuated at a temperature correspondingly high.

Attenuation by Compressed Oxygen.

95. **Paul Bert** showed that oxygen under a pressure of from 20 to 40 atm. exerts a fatal influence upon the bacillus of anthrax.

Wosnessenski (No. 40, xcviii. 1884, p. 314) conceived the idea that if a minor amount of pressure were exerted, the bacillus might become less virulent without being destroyed. He found that when anthrax bacillus is cultivated in a thin layer of *bouillon* at a temperature of from 42° to 43° C., and under a pressure of *from* 4 *to* 6 *atm.*, it is rendered inert, but is not deprived of its vitality. So attenuated does it become that it will not kill even a guinea-pig. He further alleges that *heat* has not the same attenuating effect when the organism is subjected to a pressure of 20 atm.

Chauveau (No. 40, xcviii. 1884, p. 1232), under whose superintendence they were commenced, continued these researches, finding that anthrax virus attenuated by oxygen compressed to a degree insufficient to destroy its vitality, acts as a vaccine for sheep. It can be afterwards cultivated in its attenuated condition under normal pressure and at a temperature of +36° to +37° C. The exact degree of pressure necessary to effect the attenuation had not been accurately ascertained at that time.

In a later communication (No. 40, ci. 1885, p. 45) he gives the results of the use of anthrax attenuated by compressed oxygen. He judges of the strength of virus necessary to inoculate the sheep, ox, or horse by its effect on the guinea-pig. The guinea-pig being so much more susceptible to anthrax than these animals, it follows that a vaccine which will not prove fatal to it, or which will prove fatal only in a few cases, may be employed with impunity in them.

He has inoculated large flocks of sheep in districts in which anthrax has broken out in a virulent form, and has cut the epidemic short with almost incredible rapidity. The dose for a sheep is one drop, inoculated on the ear or tail, and one to two drops for the ox or horse. A single inoculation is sufficient. The virus retains its efficacy even after six months' time.

He regards the change undergone by the bacillus as of the nature of a degeneration susceptible of being transmitted hereditarily, and with a tendency to revert to the original type (No. 40, ci. 1885, p. 142).

Attenuation by Chemical Reagents.

96. It has been alleged by Toussaint, and Chamberland and Roux, that the pathogenic effects of anthrax and other virulent organisms become attenuated when the organisms are retained in contact with dilute carbolic acid for twenty-four days at 35° C. Chromic and sulphuric acids have been held to possess similar properties.

Klein (No. 161, 1886, p. 441) has endeavoured to attenuate anthrax by growing it on *nutritive gelatine medicated with* 1 *to* 40,000 *corrosive sublimate.* The bacillus grew luxuriantly and was barren of all virulence, but this held good only so long as it was cultivated on the medicated gelatine. It was morphologically unaltered.

The bacilli of swine fever and of septicæmia of the mouse were unaltered in their virulence by this method of treatment.

Attenuation by Exposure to Sunlight.

Arloing (No. 4, vii. 1886, p. 209) states that anthrax exposed to a bright sunlight in a liquid medium gradually loses its poisonous qualities.

Literature on Attenuation of Virus.—**Bouchardat** (Principal Modes of Attenuating Virus): Rev. Scient., 1881, ii. p. 458. **Chamberland:** Le charbon et la vaccination charbonneuse d' après les récents traveaux de M. Pasteur, 1883. **Chauveau** (Attenuation of Charbon by Heat): Compt. rend. Acad. d. Sc., xciv. 1882, p. 1694; *also, Ibid.*, xcvii. 1883, p. 1397; *also,* Vet. J. and Ann. Comp. Path., xvii. 1883, p. 255; *also,* Presse vet., iv. 1884, p. 81; *also,* Recherches sur l'application de l'attenuation de Virus par la Chaleur, etc., 1884; *also* (Method of Inoculating Sheep), Compt. rend. Acad. d. Sc., xcvii. 1883, p. 1242; *also* (Attenuation of Anthrax by Compressed Oxygen), Compt. rend. Acad. d. Sc., xcviii. 1884, p. 1232; *also,* Rev. Scient., x. 1885, p. 614; Rev. de Méd., vii. 1887, p. 177. **Cornevin:** Premiere étude sur le Rouget du Porc., 1885. **Greenfield** (Anthrax): Journ. R. Agricultural Soc., xvi. 1880, pt. i. p. 273. **Koch, Gaffky, and Loeffler** (Anthrax): Mittheil. a. d. k. Gesundheitsamte, ii. 1884, p. 147. **Löffler** (Question of Immunity), Mittheil. a. d. k. Gesundheitsamte, i. 1881, p. 134; *also* ("Rothlauf" of Pigs), Arbeiten a. d. k. Gesundheitsamte, i. 1885, p. 46. **Lydtin and Schottelius:** Der Rothlauf d. Schweine, 1885. **Pasteur** (Chicken Cholera): Compt. rend. Acad. d. Sc., xci. 1880, p. 673; *also,* Sur la Choléra de Poules, etc.; *also* (Attenuation of Virus), Rev. Scient., iv. 1882, p. 353; *also,* Med. Times and Gaz., 1880, ii. p. 572; *also* (Charbon Vaccination, etc.) Bull. Acad. de Méd., xii. 1883, p. 586; *also* (Reply to Koch), Rev. Scientifique, xxxi. 1883, p. 74. **Pasteur and Thuillier** (Vaccination for Rouget des Porcs): Compt. rend. Acad. d. Sc., xcvii. 1883, p. 1163. **Pourquier** (New Method of Attenuating the Virus of Variola Ovina): Compt. rend. Acad. d. Sc., ci. 1885, p. 863; *Ibid.*, civ. 1887, p. 703. **Salmon** (Attenuation of Virus): N. Y. Med. Rec., xxii. 1883, p. 370. **Sanderson** (Anthrax): Journ. R. Agricultural Soc., xvi. 1880, pt. i. p. 267. **Schutz** ("Rothlauf" of Pigs): Arbeiten a. d. k. Gesundheitsamte, i. 1885, p. 56. **Ziegenhorn** (Attenuation of Pathogenic Fungi): Arch. f. exp. Path. u. Pharmakol, xxi. 1886, p. 249.

Attenuation of Pathogenic Moulds.

97. Ziegenhorn (No. 104, xxi. 1886, p. 249) has attempted, but without success, to attenuate pathogenic moulds such as *Aspergillus fumigatus* and *Mucor rhizopodiformis.* Fraenkel (No. 93, 1885, p. 546) believes that the moulds differ from the cleft fungi in so far as their pathogenic properties appear to be incapable of modification

Immunity from Contagious Disease.

98. **Natural Immunity.**—Certain animals are naturally protected from the ravages of some of the most virulent contagia. Thus *Algerian sheep* are persistently refractory to anthrax when inoculated in the usual way. *Dogs* and *rats* are with difficulty inoculated, and *birds* are almost completely exempt.

Age appears to exert considerable influence on the susceptibility to inoculation. Young animals, as a rule, are more readily inoculated than old.

The dose of the poison is also a most important consideration. Chauveau (No. 40, lxxxix. 1879, p. 498) discovered that although

Algerian sheep are refractory to anthrax inoculated through a scratch in the skin, yet that they fall victims to the disease when the quantity injected is increased. The same appears to hold good for many other organisms. As Cheyne expresses it (No. 6, 1886, ii. p. 206), the pathogenic dose of a virus varies inversely with the predisposition of the animal to the disease in question.

The particular time at which the inoculation is made also exerts considerable influence upon the success of the procedure. Rats are more sensitive to anthrax on some days than on others.

The normal temperature of the animal would appear to be the cause of failure to inoculate in some cases. Pasteur states (No. 153, 1878, pp. 253, 737; *Ibid.*, 1879, p. 1222) that a *fowl*, whose normal temperature is 42° C., if inoculated with anthrax and kept submerged in water at 25° C., dies in from thirty to forty hours of anthrax, its blood teeming with the bacillus.

The ptomaines and aromatic products secreted by pathogenic organisms appear to exert in many instances a suicidal effect upon the organisms themselves. Thus Wernich (No. 13, lxxviii. 1879, p. 51) concludes that so far at least as regards the organisms of putrefying muscle, the aromatic substances secreted by them reflect a deadly influence upon the organisms themselves. The introduction of small quantities of these poisons into culture media prevents the growth of bacteria similar to those which have generated them.

Carbolic acid is among the poisonous substances resulting from putrefaction (Baumann, No. 187, i. 1877-78, p. 60). It has long been recognised (Hoppe-Seyler, No. 169, v. p. 470) as a constituent of healthy urine, and was supposed by Baumann (*loc. cit.*, p. 61) to result from putrefaction in the intestinal canal, and to be subsequently absorbed into the circulation.

Indol and skatol are also developed during putrefaction, but have little deleterious effect on anthrax spores (Koch, No. 44, i. 1881, p. 267).

It has been asserted that the principle underlying **Pasteur's treatment of rabies** is that a *poisonous ptomaine* or other allied product is generated in the spinal cord of the rabbit, which, when injected in quantity during the stage of incubation, prohibits the growth of the supposed germ of the disease.

Why it is, however, that a single attack of syphilis, small-pox, anthrax, etc., so often confers immunity on the individual for the remainder of a lifetime is as yet unexplained.

DISINFECTION.

(1) *OF THE BLOOD.*

99. When a pathogenic micro-parasite has once taken hold of the system there is little evidence to show that disinfectants are of much

use in destroying it. Probably the nearest approach to anything of the kind is the action of *quinine in ague* and *iodide of potassium in chronic syphilis*. But how these drugs act is as yet far from being understood.

Koch (No. 44, i. 1881, p. 272) states that **quinine** hinders the development of anthrax bacilli when in solution 1 to 830, and completely prevents it when in the proportion of 1 to 625. Moczutkowsky (No. 93, 1879, No. l., quoted by Koch) calculated that 12 to 16 grm. would be necessary to destroy the spirochætæ in the blood of a patient suffering from relapsing fever. **Iodine** begins to interfere with the growth of anthrax bacilli when in solution 1 to 5000. To act, therefore, as a germicide in the blood of a person suffering from anthrax, it would require to be present to the extent of something like 12 grms. of iodine, which, of course, is an impossibility (Koch, No. 44, i. 1881, p. 268).

Attempts have been made to render animals refractory to anthrax by drugging them with **corrosive sublimate**. Koch (No. 44, i. 1881. p. 280) met with no success, but regards the matter as not yet worked out. Cash (No. 161, 1884, p. 200) found that anthrax bacilli developed in the blood but in small quantity.

Sodium sulpho-carbolate has been administered by Brakenridge as a prophylactic to individuals exposed to the infection of *scarlet fever* (No. 185, 1875, ii. p. 92). He affirms that signal success attended its administration, although of course there are self-evident difficulties in the way of drawing conclusions from such experiments. Sansom (No. 364, p. 330) found that patients could readily stand twenty to sixty grain doses. The breath assumes a distinct carbolic acid odour, the salt being evidently decomposed in the blood or tissues.

Its powers as an antiseptic, according to Klein (No. 161, 1884, p. 189), are feeble. Solutions of 10, 5, 2, or 1 per cent, have no effect in destroying anthrax bacilli. **Phenyl-propionate of soda**, according to the same authority, is more powerful.

Cash (No. 161, 1884, p. 193) found sodium sulpho-carbolate to be inert as a prophylactic against tuberculosis in guinea-pigs.

(2) *OUTSIDE THE BODY.*

100. **Method of Experiment.**—The efficacy of a disinfectant or rather a germicide, as Koch remarks, must be tested by (1) its action upon the organism when sporing; (2) by its action when not sporing; (3) by its power of preventing the growth of the organism in nutritive fluids (No. 44, i. 1881, p. 245).

A disinfectant which will destroy anthrax in the *bacillar stage* of development for instance, may prove to be quite inadequate for the purpose when applied to the *spores*. Thus Koch found (No. 44, i. 1881, p. 266) that many so-called germicides were useless against the spores of anthrax, among which he enumerates hydrochloric acid (2 per cent), sulphuric acid (1 per cent), saturated solution of chloride of

sodium or of chloride of calcium, chloride of iron (5 per cent), boracic acid, borax, chlorate of potash, benzoic acid, and quinine.

Coloured organisms such as *micrococcus prodigiosus* or the bacteria of blue pus (Koch), and anthrax bacillus and spores are the best to work upon. The former grow readily on potato and betray their presence by their colour. The latter grows so characteristically in agar-agar that it can be easily recognised. Its inoculability is also a sure means of detection.

Corrosive Sublimate.

A solution of the strength of 1 to 5000 destroys the vitality of all spores in a few minutes (Koch, No. 44, i. 1881, p. 277). A 1 to 1000 solution is probably the most useful and effectual disinfectant for general use.

Max Schede (No. 114, Chirurg., No. lxxviii. p. 2115) finds that a 1 to 1000 solution of corrosive sublimate can be employed for all surgical purposes without danger, and even for washing out cavities such as those of the chest in empyema, echinococcus cysts, etc. The employment of a 5 or 3 per cent solution of carbolic acid is attended with much greater risk of toxic effects. He considers the former solution a far more powerful antiseptic than the latter.

As a result of the use of sublimate solution he has occasionally, but only very seldom, seen an eruption similar to that of scarlet fever. The circumstances under which toxic effects are liable to ensue, are where it is employed in anæmic individuals for operations exposing a large surface, or where its use is continued for weeks at a time.

Thymol.

101. Thymol perhaps ranks next in efficacy as a chemical disinfectant. Wernich (No. 13, lxxviii. 1879, p. 62) says that 0·5 per 1000 of water hinders the putrefaction of muscle.

Carbolic Acid.

102. This is not nearly so powerful a disinfectant as is generally imagined. Koch (No. 44, i. 1881, p. 242) states that a one per cent solution in water has no deleterious effect on **anthrax spores** even after fifteen days' contact. A 2 per cent solution delays their growth but does not otherwise interfere with their vitality. A 3 per cent solution partially destroys **anthrax threads** in three days and **anthrax spores** completely in seven days. A 4 per cent solution destroys anthrax spores in three days, and a 5 per cent solution in two days. Where the fluid containing the organisms holds **albumin** in solution he reckons that a 10 per cent solution is necessary to destroy them, and therefore throws much doubt on the practical utility of carbolic acid.

The above results closely correspond with those obtained by Jalan

de la Croix (No. 104, xiii. 1881, p. 175) with the organisms of putrefying muscle.

Flügge (No. 359, p. 545) found that a 5 per cent solution of carbolic acid disinfects **phthisical sputum** with certainty in twenty-four hours.

The general supposition that a 2 per cent solution of carbolic acid is sufficient to disinfect **hands, instruments,** etc., in a few minutes seems to be entirely erroneous.

When dissolved in Oil or Alcohol it does not appear to have the least disinfecting properties (Koch, No. 44, i. 1881, p. 251); but it is possible that when dissolved in oil some of it is given up, in the case of its application to a wound, to the liquids of the tissues. Upon instruments, silk, catgut, etc., carbolic oil does not appear to have the slightest disinfecting powers even with organisms of weak vitality. Pure oil might as well be employed.

In the form of Vapour along with steam at a temperature of 75° C., and even as low as 55° C., it is thoroughly destructive of all spores. The lower the temperature the longer time is required to effect the end in view.

Carbolic Spray of the strength of 1 to 2 per cent has no effect upon the spores of various bacteria. Hence the presence of bacteria in wounds subjected to its influence may be accounted for (Koch, No. 44, i. 1881, p. 252).

Chloride of Zinc.

103. Anthrax spores are not affected by a 5 per cent solution after a month's contact (Koch, No. 44, i. 1881, p. 262). When sown on blood-serum containing from 1 to 5 per mille of chloride of zinc, anthrax spores elongate into threads within twenty-four hours. It may, therefore, be regarded as being almost inert.

Sulphurous Acid.

104. This seems to be a much more uncertain disinfectant than is usually supposed.

Chlorine, Bromine, and Iodine.

105. Cash (No. 161, 1886, p. 425) concludes that the disinfecting properties of these three substances do not materially differ from each other, except that they are capable of arrangement as regards their activity in the reverse order to the above.

Chloral Hydrate.

106. A solution 1 to 1000 retards the growth of anthrax, but even at 1 to 400 does not entirely prevent it (Koch, No. 44, i. 1881, p. 272).

Common Salt.

107. When of strength 1 to 64 it retards the growth of anthrax, but even at 1 to 24 does not prevent it (Koch, No. 44, i. 1881, p. 273).

Phenylpropionic and Phenylacetic Acids.

108. Klein (No. 161, 1883, p. 111) found these to be powerful disinfectants. A solution of 1 to 3200 phenylpropionic acid kills anthrax bacilli with certainty after thirty to thirty-five minutes. Phenylacetic acid, of the same strength, requires at least thirty-five minutes to be effective. Solutions of either of them, of the strength 1 to 200, kill all bacilli whencesoever derived. Anthrax spores, however, do not lose their virulence in these solutions, even up to two or more days, when inoculated in the guinea-pig.

Ozonised Air.

109. Grossmann and Meyerhausen (No. 169, xv. 1877, p. 245) stated that it arrested the movement and development of putrefactive microphytes, but M'Kendrick and Coleman's experiments (No. 361, 1885, p. 1058) prove that it has no effect in preventing their development in egg albumin. Spillmann (No. 187, iv. 1880, p. 350) found that it was harmless with anthrax bacillus; while Cash (No. 161, 1885-86, p. 193), working with improved facilities, found that ozone, when strongly concentrated, destroyed the vitality of anthrax bacillus but not of the spores.

110. **Action of Heat.**—For particulars see p. 122.

Action of Cold.—Extreme cold (83° C. for 100 consecutive hours) does not appear to have any effect as a sterilising agent (M'Kendrick, No. 241, 1884-85; *also*, No. 32, i.).

111. **Comparative Value of Chemical Disinfectants.**—For tabulated statements, consult the works of De la Croix, No. 104, xiii. p. 250; Koch, No. 44, i. p. 263; Bucholtz, No. 104, iv. p. 80; and Flügge, No. 359, p. 529.

DISINFECTION OF ORGANISMS OF SUPPURATION.

112. A very interesting series of experiments has lately (No. 13, cxii. 1888, p. 341) been made by Martens upon the action of antiseptics on the organisms of suppuration (*staphylococcus pyogenes aureus, albus*, and *citreus*, and *streptococcus pyogenes*). As an antiseptic, **iodine** stands pre-eminent; it is the only substance which acts deleteriously in a solution of 1 to 10,000. As a surgical application it has, however, been found inconvenient from its irritating effects, from its liability to become absorbed, and for other minor reasons. Davaine and Koch likewise found it to be a most powerful antiseptic.

Iodoform if shaken over a gelatine surface, does not prevent the growth of micrococcus *p. aureus* or *m. prodigiosus*. They continue to liquefy the gelatine but do not secrete their colouring matters. He suggests that it may, however, *prevent the formation of the ptomaines* of septic cocci, that is to say, may serve to convert pathogenic cleft fungi into those which are non-pathogenic.

Iodide of potassium seems to have very little influence.

Thymol has a deleterious action in the proportion of 1 to 5000. It seems to be very much less powerful as an antiseptic when dissolved in alcohol than in water. Both oil and alcohol, when employed as solvents, seem to interfere with the action of most antiseptics.

The following substances act deleteriously in the proportion of 1 to 1000:—**Eau de Javelle** (chiefly hypochlorite of potash), **nitrate of silver, mineral acids, corrosive sublimate, benzoic acid,** and **salicylic acid.**

Perchloride of iron, chlorate of potash, acid sulphate of potash, carbolic acid, permanganate of potash, quinaline (antifebrine), **chloride of copper, resorcin,** and **acetate of alumina** act deleteriously when of the strength of 1 to 100.

Acetic acid and **oil of turpentine** require to be in the proportion of 2 to 100; while **chloride of zinc** will prove deleterious when the strength is 5 to 100.

A great deal seems to depend upon the **time** during which the antiseptic is in contact with the organism. Thus a 4 per cent solution of boracic acid proves an effectual germicide only after ten days.

Literature on Disinfection.—**Bucholtz** (Antiseptics and Bacteria): Arch. f. exp. Path. u. Pharmakol., iv. 1875. **Cash** (Certain Chemical Disinfectants): Rep. Loc. Gov. Board, Suppl., 1884, p. 192; (Chemical Substances as Prophylactics) *Ibid.*, 1884; (Oxygen and Ozone as Disinfectants) *Ibid.*, 1885, p. 193. **Cornil et Babes:** Les Bactéries, 1885, p. 44. **De la Croix:** Arch. f. exp. Path., xiii. 1881, p. 175. **Fischer:** Article in Neuen Handwörterbuch d. Chemie. **Fischer and Proskauer** (Chlorine and Bromine): Mitth. a. d. k. Gesundheitsamte, ii. 1884, p. 228. **Förster** (Hands): Centralbl. f. klin. Med., No. 15, 1885. **Frisch** (Influence of Temperature): Sitzungsb. d. k. Wien. Akad., lxxv. and lxxx. **Hüppe** (Ferments and Temperature): Mittheil. a. d. k. Gesundheitsamte, i. 1881, p. 341. Instructions for Disinfection, prepared for the National Board of Health, N. Y., 1879. **Klein** (Phenylpropionic and Phenylacetic Acids, Chlorine): Rep. Loc. Gov. Board, Suppl., 1883, p. 111; (Air Disinfection) *Ibid.*, 1884, p. 187; (Phenyl Acids and Salts) *Ibid.*, 1884, p. 188. **Koch** (Disinfection): Mittheil. a. d. k. Gesundheitsamte, i. 1881, p. 234, **Koch, Gaffky, Löffler** (Disinfection with Steam): Mittheil. a. d. k. Gesundheitsamte, i. 1881, p. 322. **Koch and Wolffhügel** (Hot Air): Mitth. a. d. k. Gesundheitsamte, i. 1881, p. 341. **Lebedeff** (Malignant Œdema): Arch. de Physiol. norm. et pathol. x. 1882, p. 175. **Martens** (Antiseptics): Arch. f. path. Anat., cxii. 1888, p. 341. **M'Kendrick** (Effect of Extreme Cold): Text-book of Physiology, 1888. **Neisser** (Iodoform): Arch., f. path. Anat., cx. 1887, pp. 281, 381. **Pictet and Young** (Action of Cold): Compt. rend., xcviii. 1884, p. 747. **Proskauer** (Value of Sulphurous Acid in Air): Mittheil. a. d. k. Gesundheitsamte, i. 1881, p. 283. **Sanderson** (Infection and Disinfection): Rep. Loc. Gov. Board, Suppl., 1882, p. 213; (Products of Putrefaction in Relation to Disinfection) *Ibid.*, 1883, p. 101; *Ibid.*, 1884, p. 183. **Schede** (Corrosive Sublimate): Sammlung klin. Vorträge, No. 251, 1885. **Schill and Fischer** (Disinfection of Phthisical Sputum): Mitth. a. d. k. Gesundheitsamte, ii. 1884, p. 131. **Steinmeyer:** Ueb. Desinfectionslehre, 1884. **Tyndall:** Philosoph. Trans., clxvii. 1877, p. 149. **Vallin:** Traité des désinfectants et de la désinfection, 1883. **Wernich** (Action of Aromatic Products of Putrefaction on Vegetable Micro-Organisms): Arch. f. path. Anat., lxxviii. 1879, p. 51. **Wolff:** Centralbl. f. d. med. Wissensch., xxiii. 1885, p. 177. **Wolffhügel** (Disinfection with Hot Air): Mittheil. a. d. k. Gesundheitsamte, i. 1881, p. 352 (Sulphurous Acid) Mitth. a. d. k. Gesundheitsamte, i. 1881, p. 188. **Wolffhügel and Knorre** (Carbolic Acid): Mitth. a. d. k. Gesundheitsamte, i. 1881, p. 352.

Testing of Air for Germ Impurities.

113. Various means have been adopted for this purpose. In the older instruments, liquid media were employed. They are not nearly so serviceable as those which are gelatinised.

Miquel's Apparatus (No. 365, pp. 138 and 175). A ballon (*b*) of 50 c.c. capacity is blown on a tube *af*, the latter being bent as in the figure. A plug of asbestos is placed at each of the points *d*, *c*, and the tube is drawn out between them. The apparatus is sterilised with dry heat and about 20 c.c. of a liquid nutritive medium (bouillon) are collected in the ballon (*b*) by dipping the point *a* in the medium and aspirating at *f*. The point *a* is then dried and sealed in a flame.

FIG. 52.—MIQUEL'S APPARATUS FOR TESTING THE GERM-IMPURITY OF THE AIR.

In using it, the part *cd* is inclined at an angle of about 25°, and the point *a* is correspondingly elevated. The end *f* is connected to a graduated aspirator by means of an india-rubber tube. The point *a* is broken with sterile forceps. A measured quantity of air is drawn through the apparatus by means of the aspirator, and immediately afterwards the point *a* is again sealed in the flame. By vigorous blowing the plug *c*, which probably contains some germs, is displaced and driven into the liquid, and, by inclining the apparatus, the liquid is allowed to penetrate to the point *a*, so as to absorb any germs in this part.

Large numbers of the flasks are used in a single observation. The results do not show directly how many germs are contained in a given bulk, but merely how many of the flasks become contaminated by the measured samples of air aspirated.

Hess's Method (No. 44, ii. 1884, p. 182). This essentially consists in employing an apparatus by which a measured quantity of air may be aspirated through a long glass tube whose interior is coated with nutritive gelatine. The germs fall on the lower surface of the tube, and can be counted as they begin to form colonies.

The apparatus is composed of a glass tube 70 cm. in length, with a bore of 3·5 cm. The end is covered with an elastic cap, having a round aperture, 1 cm. diameter, in its centre. This first cap is covered by a second without any central aperture, which completely closes the end of the tube. The other end of the tube is fitted with a caoutchouc cork and central tube, 1 cm. bore, and 10 cm. long. The central tube is connected with two aspirating bottles by means of elastic tubing. Two cotton plugs are

driven into the glass tube perforating the cork, the one at the proximal end, the other at a short distance from it.

FIG. 53.—HESS'S APPARATUS FOR COLLECTING GERM-IMPURITIES OF THE AIR.

In charging it, take out the cork and introduce 50 c. c. nutritive gelatine. Replace the cork, and subject the apparatus to steam heat, in the steam steriliser, for from one to two hours. Remove it, and when so cool that one can hold it in the fingers without inconvenience, rotate the tube in such a manner as to coat the whole of its interior with a thin film of the gelatine. The floor ought to have the thickest coating, as it is here that the germs mostly fall. The rotation is done under a stream of water. The tube must then be left at rest for several days in order to prove the sterility of the gelatine.

When about to be used, attach the aspirator, take off the outer elastic cap from the end, and draw the air through very slowly. Note the quantity of water used in aspirating. A litre is that generally selected, and of course the quantity ought to be alike in all comparative observations.

Ordinary bacteria usually alight at the anterior part of the tube, *spores* of fungi at the posterior. Hess alleges that the reason of this is that the bacteria are held together in masses, while the spores are free.

The chief objections to the apparatus are said to be, that it does not catch all the germ impurities, and that the spores do not all begin to grow when they fall on the gelatine surface. It is, however, highly recommended by Carnelly, Haldane, and Anderson (No. 65, clxxviii. 1887, p. 65), and others, who have employed it largely on account of its simplicity and fair accuracy.

Pawlowsky (No. 43, xxii. 1885, p. 330) endeavours to render an apparatus constructed on the same principle a more thorough germ-trap by bending the tube in a series of angular curves.

A still simpler method, which the author has frequently

employed and found effectual, is as follows. A large number of sterile glass capsules, similar to those recommended for potato (Sect. 63), are each charged with sufficient nutritive gelatine to form a layer about $\frac{1}{8}$ in. thick on the bottom. The lids are fastened down by means of a couple of elastic bands or with thin wire, and the capsules and their contents are all sterilised with steam in the usual manner (Sect. 69). An interval of a few days is allowed to elapse, so as to ensure that those selected are sterile. They are then packed in sterile cotton, and conveyed to the locality in which the atmosphere is to be tested. The capsules must be all of the same size, and at least $2\frac{1}{2}$ inches in diameter.

The lid is removed with the greatest care in the particular site selected, and in all cases the gelatine is exposed for the same time (20 minutes). Before removing the lid, however, it is well to dip the floor of the capsule for an instant into hot water. The small quantity of gelatine so melted should be allowed to run over the surface of the mass in the finest film. The spores and bacteria which fall upon it are thus enabled to take better hold and to grow with greater certainty. A large number of capsules must be used at each observation for the purpose of comparing results. The air should be as still and undisturbed as possible in the apartment where the observation is being made.

FIG. 54.—VACHER'S INSTRUMENT FOR COLLECTING IMPURITIES OF EXPIRED AIR.

The advantages which the author claims for this method are its simplicity, the exclusion of any probable source of fallacy from accidental contamination, the ease with which the colonies can be examined and transferred to fresh media, and the absence of all necessity for aspiration.

COLLECTION OF GERM IMPURITIES IN EXPIRED AIR.

114. Different means have been adopted for this purpose, the best principle apparently being that of bringing the expired air in contact with a surface coated with some viscid material.

Vacher's apparatus (No. 59, 1883, i. p. 633) consists of a metal cap fitting tightly over the mouth by means of a readily inflated air cushion. The cap has two apertures, one at the side, provided with a valve opening inwards; the other in front, having a cover-slip coated with albumin held close behind it by two clips. The expired air impinges against this, and after several expirations have been made,

the albumin is dried and the organisms stained and mounted as before directed (p. 139).

Collection from Air generally.—Many ingenious instruments have been invented by Pasteur, Pouchet, Maddox, Cunningham, and others. That of Pouchet (Fig. 55) is extremely simple, and is designed, as many of the others are, to cause the air to impinge against a glass

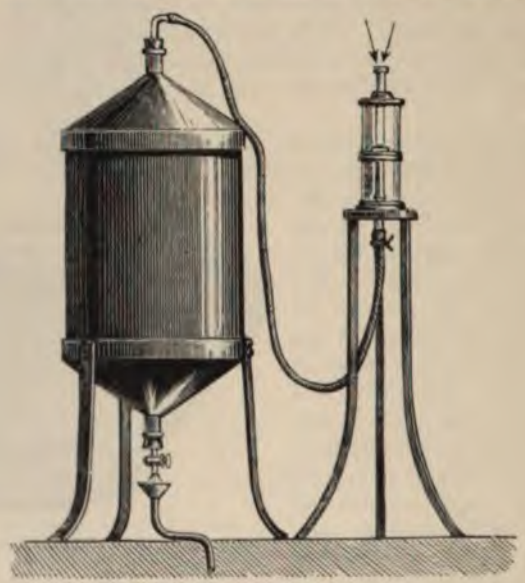

FIG. 55.—POUCHET'S AEROSCOPE.

slide having some viscous substance adhering to it. It consists of a cylinder filled with water, having an escape-pipe below. Connected with the roof of the cylinder is an elastic tube in communication with a glass chamber containing the slide. The aspiration of the water causes a stream of air to enter in the direction of the arrows.

Literature on Testing Air for Germ-impurities.—**Carnelley, Haldane, and Anderson:** Phil. Trans., clxxviii. 1887, p. 61. **Cunningham:** Microscopical Examination of the Air; Calcutta, 1874. **Emmerich:** Arch. f. Hygiene, i. Heft 2. **Frankland** (Method): Ztschr. f. Hyg., iii. 1887, p. 287. **Freudenreich** (Air of Mountains): Rev. scientif., ii. p. 384. **Hache:** Rev. de Chir., iv. 1884, p. 462. **Hesse** (Quantitative Analysis of Micro-organisms): Mittheil. a. d. k. Gesundheitsamte, ii. 1884. p. 182. **Klebs and Tommasi-Crudeli** (Malarious Air): Arch. f. exper. Path., xi, 1879. **Koch:** Mittheilungen a. d. k. Gesundheitsamte, i. 1881, p. 32. **Miflet:** Cohins Beitr. z. Biol. d. Pflanzen., vol. iii. **Miquel:** Les organismes vivants de l'atmosphère, 1883. **Olivier** (Germs of Air): Rev. scient., xxxi. 1883, p. 290. **Thèse:** Rev. scient., 1883. **Pawlowsky** (New Apparatus): Berl. klin. Wochnschr., xxii. 1885, p. 330. **Smart:** Germs, Dust, and Disease, 1883. **Tyndall:** The Floating Matter of the Air in Relation to Putrefaction and Infection, 1881. **Vacher** (Instrument for Collecting Exhaled Germs): Lancet, 1883, i. p. 633.

Bacteriological Investigation of Water.

115. Koch's method of fractional cultivation has been much utilised for this purpose (No. 44, i. 1881, p. 36), more especially Esmarch's modification of it (Sect. 73). The water is received in a sterile vessel, and, with a sterile pipette 1 c.c. of it is transferred into a test-tube containing 10 c.c. of nutritive gelatine at the lowest temperature compatible with the latter remaining liquid (about 30° C.) This is then spread out in the interior of the tube, the flat tube recommended by Arloing (Sect. 73) being particularly suitable.

If the bacteria are very abundant, a fraction of 1 c.c. may be substituted.

The colonies are counted as they begin to grow, and a corresponding calculation made. Fol (No. 367, xiii. 1885, p. 110, quoted by Hueppe) alleges that only 4 per cent of all germs fructify in the gelatine, and that hence to obtain the actual number present it is necessary to multiply by 25. Hueppe (No. 363, p. 231) coincides with this view.

If the colonies liquefy the gelatine rapidly, **agar** should be substituted. Water for analysis should be transported in sterile stopper bottles covered by a caoutchouc cap.

It must be added that a large number of observations should be made of each sample, and that the result should be the average of these. The colonies should also be cultivated at different temperatures, and plenty of time (a fortnight at least) should be allowed to elapse before the counting of the colonies is completed.

Testing of Water.—**Arloing** (Bacteriological Analyser for Water): Arch. d. Physiol. norm. et path., x. 1887, p. 273 **Becker**: Anleitung zur Untersuchung. des Wassers auf Mikroorganismen. **Bischof** (Koch's Bacteriological Water Test): Lancet, 1885, ii. p. 382; *Ibid.*, 1887, i. p. 726; *Ibid.*, 1887, ii. p. 516. **Chamberland** (Physiologically Pure Filter): Compt. rend., xcix. p. 247. **Frankland** (Vitality of Pathogenic Micro-organisms in): Lancet, 1886, ii. p. 226. **Hesse** (Water Filtering): Deut. med. Wochnschr., 1885, No. 5. **Koch**: Mittheilungen a. d. k. Gesundheitsamte, i. 1881, p. 36. **Smith** (Testing by Koch's Gelatine): San. Rec., Lond., iv. 1882, p. 344.

PART II

GENERAL PATHOLOGICAL PROCESSES

CHAPTER X

HEALTH AND DISEASE

116. THE term **Pathology** (πάθος, disease, and λόγος, a discourse) literally means a discourse upon disease. What is disease? This can be understood only by clearly defining the meaning of the term *Health*.

Definition of Health.—*Health is that condition of structure and function of an organism which, on examination of a sufficient number of examples, we find to be commonest.*

On examining such an organ as the kidney, it is found to be made up of a capsule, medullary and cortical parts, urinous tubes, Malpighian bodies, blood-vessels, etc. These have a certain constant size, thickness, and shape, and on examination of say twenty animals of the same species, these characteristics are found to be constant. If any kidney, accordingly, of the same species, and at a like age, comes up to this standard of structure, we call that the *normal* or *healthy structure* of the kidney.

When the urine is investigated it is found to be excreted in a certain quantity, it has a peculiar colour, and contains certain organic and inorganic constituents. In a large number of instances the constituents present are found to correspond in their nature and quantity, and we consequently say that the *normal* or *healthy function* of the kidney is to excrete these in this quantity.

If other organs and parts be similarly examined, a certain standard of structure and function will be found to prevail; and if all the organs and tissues respond to this test, we designate such an individual a *healthy organism*. There is, as it were, a certain equilibrium in structure and function which is reached in each organ separately, and consequently in the animal as a whole, in what we call the *healthy* being. The terms *healthy* or *normal* are used indiscriminately to express this condition, and any departure from it is described as the *unhealthy* or *abnormal*. The definition of health is therefore purely arbitrary; it is simply the result of experience.

117. **Health and Utility.**—What we designate the normal or

healthy structure or function of an organ is not necessarily that which is of the greatest conceivable value from the utilitarian point of view. Perfection of adaptation to a purpose is no doubt one of the grand results of evolution, but it must be remembered that this perfection has not been as yet attained in all cases. We consider the brain of man as the typically perfect brain. It is, however, quite possible to conceive a being gifted with a brain of powers so vastly greater that the happy possessor would be able to transcend by far the ordinary limits of human thought. Such a condition would, however, be considered so abnormal as to be actually reckoned something morbid. We say that "genius," or the over-development of a particular faculty, "is akin to madness,"—that is, it borders upon the diseased. It is not, therefore, the highest conceivable development of structure or function which is termed health, but it is the fulfilment of *a certain constant standard* of excellence.

118. **Definition of Disease.**—The definition of disease then becomes easy. *Disease is any departure from the normal standard of structure or function of an organ or tissue.*

If, instead of the normal number of Malpighian bodies in the kidney, we find, say, only two-thirds or a half of that number, the condition constitutes *disease of structure;* and if, again, the amount of the solids or liquids discharged through the organ differs in quantity from the usual standard, or if any new product be superadded, this constitutes *disease of function.*

Growth and Development.

119. **Definition of Growth.**—*Growth is the increase in bulk of an organ or tissue by addition to the number of its cellular elements without the production of structural abnormality or differentiation into unlike tissues.*

Development is something quite different from **growth.** The ovum after being fructified divides, and soon the resulting cells begin to differentiate into unlike tissues, such as epithelium, muscle, connective tissue, nerve fibre, etc. Growth, however, commences only *after the rudiments of the organs and tissues have been laid down.* Given a certain number of cells in the primitive embryo, both its development and growth take place by division of these. There is this difference, however, between the truly growing organ and one which is merely developing, that in the former each cell reproduces its like. Liver cell gives rise to liver cell, epithelium to epithelium, and so on. There is no further transformation of cells into unlike tissues. The manner in which this cellular increase takes place in the animal body is by the successive division of the nucleus and protoplasm.

The great inequality in the bulk of animals depends upon a numerical preponderance of the cells of the one over those of the other, not upon a difference in their size. The cells of many small animals are indeed larger than those of colossal dimensions. The cells of the

fœtus are as a rule larger than those of the adult. It is alike in a growing part; the increase in bulk which occurs is numerical.

120. **Increase in bulk by increase in the size of the constituent elements.**—A tissue sometimes increases in bulk by an augmentation of the formed parts of its constituent elements. Thus the relative quantity of myosin in a muscular fibre has been shown by Zielonko (No. 13, vol. lxii. p. 29) to vary at different periods of life. In the fœtus of seven months it is smaller in amount than in that of eight; it is proportionally greater in the child of one year than in the fœtus, and very considerably larger in the adult than in the child.

The sarcous substance in the muscles of a well-fed muscular animal is more abundant than in one in poor condition (Auerbach), and yet the muscular fibres may be the same in number in the one as in the other. In a young fibrous tumour the quantity of fibre is comparatively slight in proportion to the number of the cells. As it becomes older the amount of fibre increases in quantity, and the whole mass assumes greater bulk. In plants an excess of bulk may result from an over-secretion of cellulose or starch.

Are these instances of growth? Certainly not, and for the following reasons: The sarcous substance of muscle is in reality to be regarded as the **secretion** of a muscle cell. If the muscle fibre is traced from its earliest stage of development, it looks at first like a granular precipitate thrown out round a spherical or oval-shaped cell, and its further increase in size consists in an addition to this in length and breadth. The white fibrous tissue of a tumour is similarly formed. It is at first thrown out as a secretion from a connective tissue corpuscle, and the matrix of cartilage or bone is produced in like manner. They are **secretions** from cells endowed with the property of elaborating them. The cellulose and starch of plants are also to be regarded as secretions from vegetable cells.

If, therefore, we are to look on an organ which has gained bulk by the deposition of myosin, collagen, chondrigen, or calcified bone matrix, as having grown, or if we are to regard a plant which has stored up an excess of starch or cellulose as having grown in the true sense of the word, there is no reason why we should not regard, say, a liver which has increased in bulk from a distension of its bile ducts by its proper secretion as having also grown.

There is evidently something more in a growing part than a mere storing up of excess of nutritive pabulum over expenditure. The substances just enumerated are evidence of work done. They are not, however, necessarily associated with *the calling into existence of new cells*, which is the essential of growth. In true growth, like produces like. The old and the new cells of a growing sarcoma are identical in their characters, but in the instances above enumerated of increase in size from the deposition of a secretion, nucleated protoplasm forms a substance unlike itself both in chemical composition, physical properties, and powers of reproduction. In fact the two things—growth and

secretion of a matrix—stand to each other in inverse proportion. In actively growing parts the matrix or substance secreted is small, both in the animal and vegetable kingdom. It is rather where a period of quiescence or equilibrium is reached that the matrix begins to prevail. When this stable condition has been attained, any tissue may *increase in bulk* by accumulation of matrix; it has not, however, necessarily *grown*. It is therefore clear that **increase in size** is not **growth.** It is simply one of the attributes of a growing part.

HYPERTROPHY (*ὑπέρ, in Excess, and τροφή, Nutrition*).

121. This term, like that of atrophy, is frequently employed in the loosest sense. It is extremely desirable that some strict definition be given of both of these, and that this be adhered to. It will consequently be understood that when they are employed in this work the meaning attached to them is in accordance with the definition about to be given.

The definition of health, as already detailed, is that it is the normal standard of structure and function. That of hypertrophy must be stated in terms of this.

Definition.—*Hypertrophy of an organ or tissue expresses that condition where its normal bulk is universally augmented by an additional number or by increased dimensions of its tissue elements, without deposition of a foreign substance.*

The **function** of the hypertrophied organ or tissue may be perfect or may be exalted. Of the two the latter is the commoner. The hypertrophied biceps muscle is usually more powerful than one of natural size. The hypertrophied connective tissue of an organ sustains those parts with which it is united more securely than in the normal state.

Hypertrophy, as must be apparent from the definition just given, is quite a different thing from mere **enlargement** of a part. A waxlike or a fatty liver is very large, but neither of them is hypertrophied. The cause of the enlargement in both cases is the *deposition of a foreign substance* within or among the natural constituents of the organ.

It will be noticed that in the above definition the word "universal" is employed in relation to the increased size. If the overgrowth of an organ or tissue be *local*, the term hypertrophy is not applied to the condition. If it be a gland which is concerned, such a local enlargement is designated an **adenoma,** and if a simple tissue, the name **muscular, fibrous,** or **osseous tumour** is given to it, as the case may be. A local hypertrophy is, therefore, known as a **tumour** or **neoplasm.** Thus the universal enlargement of the uterus in pregnancy is known as an **hypertrophy,** the partial enlargement of it in a myoma is called a **tumour.**

Hypertrophies are sometimes called *true* and *false*. Nothing could be more illogical. How can a thing be both true and false? Either

the part is hypertrophied or it is not, and once a strict definition is given of the condition there cannot be any doubt as to which category it belongs.

Hypertrophy of Striated Muscle is one of the best instances of the condition. It may result from two causes—overwork and increased nourishment. According to Zielonko (No. 13, vol. lxii. p. 29), the state of the muscle varies according to which of these two causes has given rise to it. Where it results from *overwork*, the growth in bulk is owing to an *increase in the number* of the muscular fibres, while if it is the result of *increased blood-supply*, the enlargement is usually due to *increase in their bulk*. The size of the individual fibres apparently does not become augmented from an increase of the work done.[1]

The compensatory enlargement of the opposite kidney, when one is removed, is often quoted as a most striking instance of hypertrophy from overwork. Yet it would seem that this enlargement is not an hypertrophy at all. There are certain kidneys which are congenitally large and single. Here the enlargement is undoubtedly due to kidney substance. The two kidneys are combined in one, while the tubes and other histological elements are of natural dimensions. This is not hypertrophy in the true sense, but simply a congenital fusion of the two organs. When, however, the one kidney is excised in an animal, or when it is destroyed in Man, the other certainly, within a very short time, enlarges, and the vulgar interpretation of this is that it has hypertrophied from overwork. Rosenstein (No. 13, vol. liii. p. 141) and others have conclusively shown that there is no real hypertrophy of the gland elements, but a mere dilatation of the blood-vessels and lymphatic spaces.

Sometimes the **connective tissue** becomes hypertrophied universally in a part or organ. This happens in the muscles of the calf of the leg in pseudo-hypertrophic paralysis, and sometimes throughout a whole hemisphere of the brain as an effect of a tumour situated in some part of it. If the increase is uniform, it may justly enough be called an hypertrophy of the connective tissue of the part.

[1] The enlargement of the uterus in pregnancy is chiefly due to a numerical increase of the muscular fibre. It is questionable what the immediate cause of the hypertrophy is. In hypertrophied arteries the increase is also numerical.

CHAPTER XI

THE INFILTRATIONS AND DEGENERATIONS

A. *THE INFILTRATIONS*

122. **Definition of an Infiltration.**—*An infiltration is a process by which a substance normally existing in the body, or foreign to it, is poured into a tissue or organ from without, which does not necessarily destroy its vitality, but merely affects it mechanically by pressure or otherwise.*

FATTY INFILTRATION.

123. **Definition.**—*By fatty infiltration is meant the production of oil in the interior of a cell from materials furnished from without.*

It is, therefore, quite a different process from *fatty degeneration* or *metamorphosis*, which implies the death of the cell or fibre affected by it and its transformation into oil.

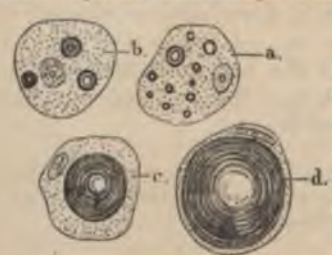

FIG. 56.—FATTILY INFILTRATED LIVER-CELLS (×400 DIAMS.)

(*a*) First stage, where the globules are small and of various sizes; (*b*) second stage, where they have partly run together; (*c*) third stage, where they have run into a single globule; (*d*) fourth stage, where this globule has distended the protoplasm of the cell.

It occurs naturally in connective tissue cells in the deposition of ordinary adipose tissue (Fleming, No. XIV. vol. vii. p. 32). According to Fleming, the carbonaceous material from which the oil is derived circulates in the blood in the form of a soluble compound. The solution leaves the vessels and soaks into the connective tissue corpuscles. They absorb it, and free oil globules are precipitated in the protoplasm of the cell.

The same process takes place *physiologically* in the liver, and it is only when it is excessive that the condition becomes pathological.

Histological Characters of a Fatty Infiltration.—Let us select for the purpose of illustration the familiar example of the fattily

Fig. 21. *Wax-like liver. Shows a lobule infiltrated with the substance examined in water, a, portal zone in which liver cells are still retained, b, waxy middle zone, c, inner zone with some remains of liver cells × 50 Diams.*

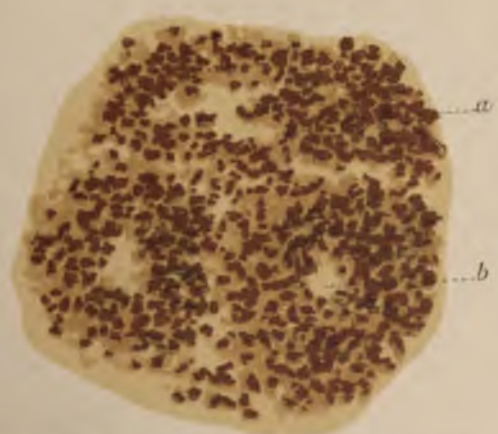

Fig. 22. *Wax-like liver stained with iodine & viewed with direct light. It shows the brown colour of the waxy masses (a) and the yellow colour of the intermediate tissue (b) × 30 Diams.*

infiltrated liver cell. The first step in this process is the appearance of several small globules of oil in the protoplasm of the cell. They are of unequal size, this being characteristic of the fatty infiltration as contrasted with the corresponding degeneration. The oil globules, in course of time, grow larger and coalesce, so as ultimately to form a single giant globule. The latter distends the protoplasm of the cell so that it is stretched round it, and pushes the nucleus to one side, where it becomes flattened from compression. The cell protoplasm may rupture and allow the oil globule to escape, but this is unusual. Even when it does so, the cell does not appear to lose its vitality, but closes in again and resumes its functions. As a rule, however, the oil becomes absorbed, and is thus got rid of without there being any rupture.

Causes.—Forced rest and an excessively rich carbonaceous diet are the commonest, but the reader is referred to the causes productive of fatty liver (vol. ii.) for a fuller summary.

The Wax-like, Lardaceous, Amyloid, or Albumenoid Disease.

124. **Definition.**—*The infiltration into an organ or tissue, of a peculiar foreign and solid substance having a composition identical with albumin.*

General Characters.—The substance gives to the infiltrated organ or tissue a peculiar dry glossy lustre, like that of a wax cast. It is hard, and hence organs infiltrated with it are peculiarly rigid. The rigidity, however, is not like that resulting from fibrous overgrowth, for the tissue is extremely elastic, and readily recoils when a depression is made upon it with the finger. The affected organ is usually, but not always, much enlarged, and its borders have an infiltrated appearance; so that the thin attenuated anterior edge of an organ such as the liver becomes more or less bluntly wedge-shaped. If the organ is small in size, the disease is usually combined with an excess of fibrous tissue.

Chemical Nature.—The wax-like substance is of high specific gravity, and does not readily decompose when exposed to the atmosphere. It is not acted upon by the gastric juice, and this circumstance has been taken advantage of by Kühné and Rudneff (No. 13, xxxiii. p. 66) for the purpose of isolating it from the surrounding parts. When isolated and pure it forms an almost snow-white precipitate which gives much the same reactions as when in the tissues. It is soluble in ammonia and in strong hydrochloric acid, but quite insoluble in dilute acetic, hydrochloric, or sulphuric acid. It does not dissolve when boiled, nor when treated with dilute solutions of potash or soda; but with a larger proportion of alkali it forms a solution and is destroyed. Its percentage composition, according to Schmidt (No. 20, cx. p. 250), and Friedreich and Kekule (No. 13, xvi. p. 50), is

$$C53 - 6, H7.0, N15.0, \& 0 \& S 24.4.$$

Gamgee (No. 21) gives the following as the average composition of albumin :—

$$C^{51.5}_{54.5}, H6.9, N15.2, O\ 20.9, \& S\ 0.3.$$

It will thus be observed that in regard to its component elements it practically corresponds with **albumin.**

Microscopically examined it is colourless, without definite structure, and translucent like obscure glass (see Pl. I., Fig. 21). Wherever it occurs it is distributed in small particles, not in large uniform masses, and it is these which, when set free by artificial digestion, impart to the residue the character of a fine precipitate.

125. **Reactions.**—It gives peculiar reactions with certain staining fluids. They are not merely *stains*, but distinct *reactions*.

(1) *Iodine.*—Solution of iodine in iodide of potassium and water gives a dark mahogany brown. The solution simply requires to be dropped over the cut surface of the organ, and allowed to lie in contact with it for half a minute, when the deep brown stain will show itself if the organ is waxy.[1]

Microscopically the characteristic dark mahogany brown colour is seen only with direct light (see Pl. I., Fig. 22). With transmitted light it appears mahogany red (see Pl. II., Fig. 23).

(2) *Iodine and Sulphuric Acid.*—When carefully applied, these reagents sometimes give a blue reaction (see Pl. II., Fig. 24). The test is extremely uncertain, however, and depends for its success a good deal upon the strength of the solutions. The majority of wax-like organs do not give a reaction with them. It is only occasionally that it is forthcoming, and hence it would seem as if the stain were due to some accidental impurity, such as **cholesterine**. On account of this blue reaction it was supposed by Virchow (No. 13, vi. p. 416) that the wax-like substance was of the nature of **vegetable cellulose** or an **animal starch,** and hence he named it **amyloid.** Vegetable cellulose, when treated with iodine, gives sometimes a brown, at other times a yellow colour. The further addition of dilute sulphuric acid strikes a blue.

Boettcher specially recommends the following procedure in order to procure the blue reaction :—

Stain the section until the reaction is evident, but not too deeply, in a solution of iodine composed of iodine, 25 grm. ; potassic iodide, 5 grm. ; water, 100 c.c. Treat it subsequently with dilute sulphuric acid of the strength of 7 to 8 c.c. to 100 c.c. of water. The great secret in obtaining the reaction is to employ the two solutions very weak. If the iodine stain is at all deep it gives a greenish hue to the section. The colour ought to be a bright azure, and is always most vivid when examined in the sulphuric acid mixture. The section should be viewed with transmitted light.

When **cholesterine crystals** are stained with iodine and subsequently treated with oil of vitriol they give a blue reaction of exactly the same tint as that which is obtained with iodine and sulphuric acid

[1] Sometimes the waxy spleen gives a perfectly blue-black stain instead of the usual dark brown. Friedreich (*loc. cit.*) describes a case of this kind.

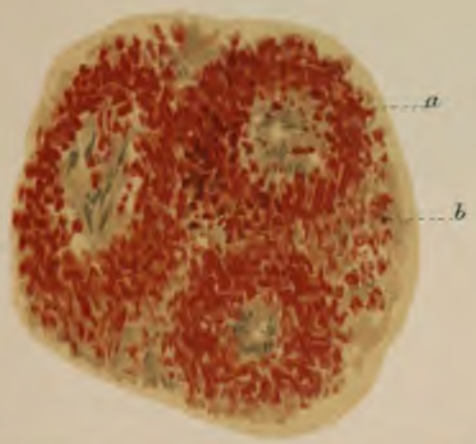

Fig. 23. *Wax-like liver stained with iodine & viewed with transmitted light. It shows the mahogany red colour of the wax-like parts (a) the dull yellow tint of those intermediate (b). x 30 Diams.*

Fig. 24. *Wax-like liver stained with Iodine & Sulphuric Acid showing the blue reaction. The disease was peculiar in this case in that the wax like substance had spread universally throughout the whole of the capillaries of the lobule. x 50 Diams.*

[redacted]

from the amyloid. The reaction commences at the edge of the crystal and spreads inwards very much as in a mass of the amyloid. Wax-like organs, moreover, contain a large proportion of cholesterine, so that in the early history of the pathology of this disease, Meckel (No. 22, iv. p. 264, 1853) was led to suppose that the wax-like substance was alike in its nature with cholesterine.

(3) *Methyl-violet*, *Gentian-violet*, or *Violet of Paris* (Jürgens, Heschl, and Cornil, Sect. 43) gives by far the most characteristic reaction. The wax-like parts stain of a rose-pink colour, while the other parts colour of different shades of purple or blue (see Pl. III., Fig. 25).

(4) *Methyl-green* (Curschmann, Sect. 43) gives a somewhat similar reaction, but the colours are not quite so brilliant.

(5) *Carmine*.—The wax-like substance readily stains with it, but does not give any distinctive reaction.

126. **Infiltration or Degeneration?**—Some years since, the disease was almost universally regarded as a degeneration of the natural cells and fibres of the part. Even so lately as the year 1878 it was maintained by Boettcher that the disease in the liver is mainly a degeneration of its cells. This view will not recommend itself to the majority of pathologists at the present day who have employed methyl-violet as a staining reagent. In no case do the liver cells seem to swell and become distended with the translucent homogeneous substance. Such might be expected were the new material a product of their degeneration. In **colloid degeneration** the accumulation of the substance within the protoplasm of the cell is readily apparent. A piece of waxy substance is sometimes seen adherent to a cell, and may be mistaken for a degeneration of the cell protoplasm. Boettcher seems to have fallen into this error. Parts which lie adjacent to a mass of amyloid frequently give the reaction at the point of contiguity, from the latter having soaked into them.

Relation of Blood-vessels to the Amyloid. — The small arteries are almost without exception the structures in which the new substance first appears. The muscular coat becomes thickened, translucent, and homogeneous; the fibres disappear from it; and the lumen of the vessel at the same time contracts (Pl. III., Fig. 25, *c*). The large arteries are usually unaffected. Soon the arterial capillaries are surrounded by the effusion, and their channels become similarly narrow.

127. **Causes.** — Exhausting suppurative diseases, pulmonary phthisis, carious necrosis of bone, and chronic syphilis seem to be peculiar in predisposing to it.

128. **Seats.**—The liver, spleen, kidney, stomach and intestine, and heart are the commonest, but it is also found in the œsophagus, muscles of the tongue, lymphatic glands, the tissue of the lung in rare cases, the skin, and occasionally in the supra renal capsules. It has been found as a tumour-like mass in the conjunctiva altered by inflammation, and as a similar mass in the tongue, as well as in tumours of bone and of the stomach.

129. **Amyloid or Colloid Bodies.**—These peculiar products are found in the central nervous system in various diseases, such as locomotor ataxia, chronic epilepsy, etc. They are usually specially abundant in the pia mater surrounding the medulla oblongata. The degenerated posterior columns of the cord, in locomotor ataxia, contain them in abundance. Similar bodies are found occasionally in various diseased conditions of the lung, particularly in emphysema. They lie embedded in the tissue of the air-vesicles. The prostatic ducts are also sometimes filled with them. They are oval or round in shape, and sometimes exhibit concentric markings like a starch corpuscle with a little cavity in the centre. They give a deep brown reaction with iodine, a bright blue with iodine and sulphuric acid, and a pink with methyl-violet (Zahn). They also colour deeply with carmine and logwood. Hot water is said to dissolve them. They appear to be of the nature of concretions, but how they are produced is unknown.

Round or oval bodies like the above sometimes originate *from contracted axis-cylinders* in the spinal cord and brain. They are described more fully under "myelitis." They must not be confounded with the former.

Artificial Amyloid.—If a spinal cord be hung up in spirit for a few months, more especially if it has not been cut into, quantities of a *material like the waxy* will be found to have formed in it. This substance is translucent and most commonly occurs in irregularly rounded masses within the white columns or gray matter. Sometimes rounded bodies, exactly like the amyloid or colloid bodies just described, become located in abundance immediately under the membranes or within the nerve roots. The nerve cells may even undergo a similar change and swell up into globular or pyriform bodies of great size. Curiously, the substance so formed gives all the reactions of the waxy, and is indistinguishable from it so far as microscopic characters go. There is not the slightest doubt that the substance is an artificial product, although it has been frequently described as something morbid.

When the degeneration is not complete the masses have a faintly granular appearance. The ordinary amyloid bodies are found in the fresh nerve centres, these are not. The pink stain which methyl-violet elicits (see Pl. III., Fig. 26) is evanescent and disappears in a few days, while in true wax-like disease it is permanent. Cells degenerate into this, but no such thing happens in amyloid.

B. *THE DEGENERATIONS.*

130. **Definition.**—*A degeneration is any process whereby a cell element or tissue undergoes such molecular changes that it can no longer maintain its functional activity, and either separates into its organic constituents or gives rise to the formation of a new product at the expense of its own substance.*

ATROPHY (*ἀ, priv., τροφή, Nourishment*).

131. Just as the term *hypertrophy* does not signify simply enlargement of an organ or tissue, so that of *atrophy* cannot be applied in logical sequence to mere diminution in size. In fact, diminution in size

Fig 25. *Wax-like liver stained with methyl aniline; a, The ring of wax-like substance, stained pink, in the middle zone; b, The surrounding liver cells stained dull blue; c, a waxy artery showing the thick homogeneous middle coat stained pink; d, branch of portal vein stained blue. × 40 Diams.*

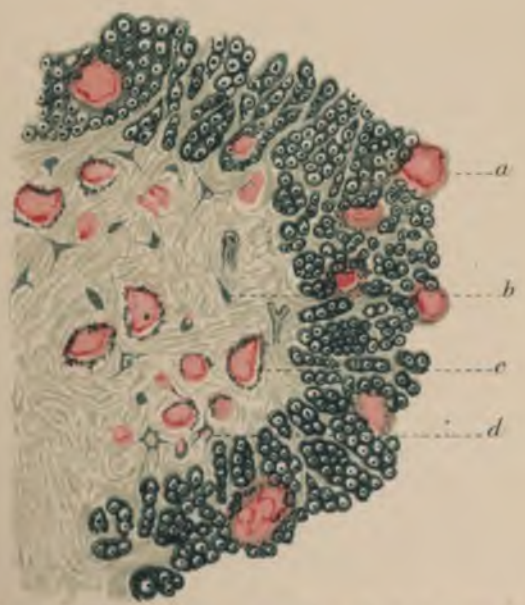

Fig 26. *Artificial wax-like substance in spinal cord; a, a mass of the substance in the white matter; b, a natural nerve cell in anterior horn; c, a nerve cell transformed into a mass of the substance; d, a nerve cell in which the substance is beginning to appear. × 50 Diams.*

is by no means a constant feature of atrophy. The wax-like liver is of huge dimensions, and yet is in a state of extreme atrophy; the fine variety of cirrhotic liver is also enlarged, but much atrophied. The diminution in size commonly seen in atrophic organs is simply one attribute of the atrophic state. If atrophy is defined as mere loss of substance, it might be argued that the vacuity left when a part is cut out with the knife constitutes atrophy. The removal of substance from many parts, commonly said to be atrophic, is effected by fatty degeneration, and although this is a natural process, still, essentially, it does not differ from removal of the part by artificial means. The loss of substance from a burn is not atrophy, but if the resulting cicatrix contract so as to exert injurious pressure and cause a limb to shrink, no one would deny that this is a true example of the process.

What definition, then, can we give of the condition? It is essential to have some clear understanding of what is meant by it, as the term is at present applied to all manner of different processes in hopeless confusion, simply because they have been accompanied by loss of substance. The author proposes, therefore, to limit the term to lesions which come under the following definition:—

Definition.—*Atrophy is the diminution in size or absolute destruction of a part which results from direct and continuous over-pressure where the blood supply is not deficient.*

It is not a direct effect of malnutrition. *Malnutrition* gives rise to *fatty degeneration*, but, in true atrophy, the parts which are consumed do not become fatty. They undergo the characteristic changes presently to be described.

It must be borne in mind that before a part can become atrophic it must have been fully developed. Arrested development is not atrophy.

The mutual pressure of the liquids and solids in the body is carefully balanced. The heart and arteries exert pressure from within; the skin, fasciæ, and muscles are sufficient to compromise this. The arterial pressure of the brain, for instance, is balanced by the counter-pressure of the cerebro-spinal fluid and the skull. There undoubtedly exists a similar balance between the arterial pressure and the tissues throughout the whole body. Under this amount of pressure they can exist, proliferate, and grow, but whenever it is augmented, either from vascular or from other causes, even although they are abundantly supplied with blood, they degenerate in a peculiar and specific manner. The term atrophy is here employed to indicate this.

FIG. 57.—ATROPHIC-LIVER CELLS FROM CYANOTIC ATROPHY OF THE LIVER IN DIFFERENT STAGES OF DEGENERATION (×400 DIAMS.)

Tissue Changes.—The changes in a cell or fibre which are characteristic of atrophy consist, in the first place, in its losing its regular outline and shrinking. The shrinking advances until the cell

is reduced to a small granular body. The granules lose their cohesion and separate; they are absorbed, and in this way the cell is removed. There is no fatty degeneration, no formation of compound granular corpuscles.

Three instances of atrophy may be quoted in which undue pressure is exerted upon the tissues, but by different agents:—Cyanotic atrophy of the liver, wax-like disease of the liver, and cirrhosis of the heart. In the first of these, pressure is exerted upon the liver cells by the distended capillaries of the hepatic vein (vol. ii.), and, notwithstanding that the blood supply is more than abundant, the cells of the organ are unable to maintain their integrity. In the second, the pressure is effected by the masses of waxlike substance; while, in the third, it is due to the contraction of the young cicatricial tissue. In none of them are the parts destroyed by fatty degeneration. Many other examples might be quoted.

FIG. 58.—ATROPHIC MUSCULAR FIBRES FROM FIBROUS MYOCARDITIS IN DIFFERENT STAGES OF DEGENERATION (×350 DIAMS.)

The cause of the atrophy in these cases undoubtedly is *pressure*, but it should be noticed that in the whole of them the pressure is continuous. Intermittent pressure, as Paget (No. 23) has pointed out, occasions hypertrophy.

CLOUDY SWELLING.

132. This degeneration was described by Virchow in the year 1847 (No. 13, i. p. 165) as occurring in various cells, more especially where the organ is in a state of what he designated parenchymatous inflammation. The various secreting and excreting epithelia and muscular fibres are most commonly affected by it.

Definition.—*A precipitation of albumin in a finely granular form in a cell or fibre by which it becomes swollen, its substance dusky, and its outline indistinct.*

Febrile states of the body accompanied by high temperature, are liable to give rise to it in muscular fibres and certain gland epithelia. It is also said that in poisoning by carbonic, phosphoric, and arsenious acids, the tissues show a similar granularity. It is most typically seen, however, in the cells of an inflamed part, such as the epithelial cells which desquamate in catarrhal affections of the kidney. In acute yellow atrophy of the liver and in acute myocarditis, the condition is also present in the liver cells and muscular fibres respectively.

The cell or fibre, when affected by the degeneration, swells and

becomes granular. The granules are very small, so that the cell assumes a finely peppered appearance. The nucleus is hidden from view, and, in the case of muscle, the striæ disappear. Acetic acid or

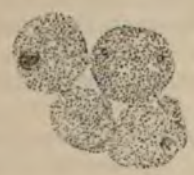

FIG. 59.—CLOUDY SWELLING OF LIVER CELLS (×350 DIAMS.)

FIG. 60.—SAME TREATED WITH ACETIC ACID.

solution of potash dissolves the precipitate and leaves the protoplasm clear and transparent. The granularity is in all probability caused by precipitated alkali-albumin.

FATTY DEGENERATION.

133. **Definition.**—*A chemical change in a cell or fibre by which it becomes destroyed from the conversion of its albumins or proteid constituents into oil.*

It must not be mistaken for fatty infiltration—a totally different process described under "Infiltrations."

Textural Changes.—When a cell or fibre is about to become fatty, the first perceptible sign of it is a cloudy swelling, an albuminous precipitate, in its substance. The albuminous particles are soon replaced by minute oil globules, few at first, but rapidly increasing in number. They are scattered throughout the cell protoplasm, and are held together simply by a little of the remains of the cell substance. As the cell becomes more and more fatty, its angles disappear and it assumes a rounded shape. At the same time it enlarges so as to form a large globular mass.

FIG. 61.—FATTY DEGENERATION. COMPOUND GRANULAR CORPUSCLES FROM A CEREBRAL SOFTENING (×400 DIAMS.)
(*a*) Ordinary form; (*b*) corpuscle disintegrating.

The name *compound granular corpuscle* is given to it when it reaches this stage. It was formerly designated an *inflammatory cell* by Gluge, but this term has now become antiquated.

The *compound granular corpuscles* are larger than the cells from which they have arisen, and hence a fattily degenerated tissue, before absorption of the fatty products has commenced, is usually bulkier than in its original state. In course of time the compound granular

corpuscles fall to pieces, and their débris is absorbed. As a consequence, of course, the part shrinks.

Causes.—(1) *Malnutrition* is the commonest, and may be local or general. Cunningham (No. 24) has shown that when tadpoles or mucorine fungi are kept in distilled water and deprived of any source of nourishment, the degeneration which follows in their tissues is of a fatty nature. When the blood becomes poor in quality, as in pernicious anæmia, the muscular fibre of the heart suffers from fatty degeneration.

(2) *Phosphorous poisoning* occasions a fatty condition of the heart and other muscular fibres, of the kidney, epithelium of the lung, peptic glands, liver, terminal arteries, etc. The process, according to Wegner (No. 13, lv. p. 2), is a true fatty degeneration—that is to say, a transformation of the albumins of the tissue into oil. It was doubtful for long whether the condition of the liver was a fatty degeneration or an infiltration. That it is a true **degeneration** of the liver substance appears now to be settled by the observations of Wegner (*loc. cit.*), Vetter (No. 13, liii. p. 168), and Meyer (No. 13, xxxiii. p. 296). In chronic cases the disease of the liver seems to end in cirrhosis. How the phosphorous acts is not known.

(3) *In child-bed* the mother sometimes suffers from an acute fatty degeneration of the tissues accompanied by jaundice. In newly-born children a similar acute fatty transformation occasionally occurs, often accompanied by uncontrollable hæmorrhage from the umbilicus.

(4) *Where a nerve fibre is separated from its trophic nerve cell* it succumbs to fatty, or, as it is called, "secondary" degeneration (see Nervous System).

Tests for the Presence of Oil in a Tissue.—(1) Glacial acetic acid or cold liquor potassæ, when applied to a microscopic section of a tissue containing oil, does not dissolve the latter.

(2) If the tissue is soaked first in alcohol, and subsequently in ether, especially boiling ether, the oil readily dissolves.

(3) Solution of perosmic acid ($\frac{1}{2}$ per cent) blackens it.

(4) The oil globules with transmitted light have a clear centre and a very dark border, so that they give to the part an almost black appearance.

COLLOID (κόλλα, *Glue or Jelly, and* εἶδος, *a Resemblance*).

134. **Definition.**—*A degeneration by which cellular structures, especially those of an epithelial type, become converted into a peculiar structureless semi-solid substance of homogeneous jelly-like consistence.*

It is particularly liable to affect epithelia lining ducts or vesicles whose outlets are naturally closed or have become so by disease. The vesicles of the thyroid body always contain some of it, and occasionally it increases so as to form a species of goitrous tumour. All cancerous tumours are subject to it, especially those of the gastro-intestinal tract.

Colloid occurs in the tubes of the kidney in various diseases, giving rise to what are known as hyaline casts. Cystic ovarian tumours sometimes contain large quantities of it.

It is either a hard gelatinous-looking substance, or, as happens in ovarian tumours, it is soft, semi-liquid, and stringy or ropy. When the degeneration affects cancerous tumours, the substance is of firm consistence, so that they cut with a clean edge. It usually has a faint bluish or yellow colour, but when perfectly pure is almost colourless.

FIG. 62.—COLLOID DEGENERATION OF THE EPITHELIAL CELLS OF A CANCEROUS TUMOUR OF THE MAMMA (×400 DIAMS.)

Microscopically examined, it is homogeneous or faintly stringy looking, and sometimes the masses present a concentrically striated appearance. The usual colloid degeneration met with in cancerous tumours appears to be entirely formed from the epithelial cells of the tumour. One or two globules of colloid are first seen in the protoplasm of the cell. These may either subsequently coalesce to form a single globule, or several moderately large globules may thus originate. The cell next falls to pieces, and the globules escape and run together. Hence, in a cancerous tumour the alveolar spaces in the stroma are filled with a clear homogeneous substance and the cells have disappeared. The stroma does not appear to suffer.

Iodine, methyl-violet, and methyl-green do not give any reaction with this substance. It stains, however, readily with carmine.

Chemical Nature.—The information regarding this is still unsatisfactory. It appears generally to be a complex and uncertain mixture of several albuminous and albuminoid substances. It sometimes contains mucin, sometimes not. Its mere presence or absence cannot be held as distinguishing this degeneration from the mucoid.

Virchow (No. 13, vi. p. 580), who first described the degeneration, came to the conclusion that, so far at least as regards the thyroid gland, it was an alkali-albumin precipitated by excess of chloride of sodium. Chloride of sodium is sometimes present in excess in the thyroid gland, and in a crystalline form (Krause).

Scherer (No. 20, lxxxii. p. 135) found a peculiar albumin-like substance in the ropy viscid fluid from an ovarian cyst which he named *paralbumin*.

Hoppe-Seyler discovered that such ovarian cysts also contain a substance giving the reactions of grape-sugar. He looks upon it as allied to glycogen.

135. **Colloid Degeneration of Muscle.**—Zenker (No. 2) has described a peculiar form of colloid degeneration occurring in muscles, especially in the adductors of the thigh and the flat muscles of the abdominal wall, in typhoid fever. It is also found, to a less extent, in the same localities in tetanus, small-pox, and scarlet fever. Bennett long ago drew attention to this degeneration as a local

process in the neighbourhood of a sarcomatous tumour. The lesion, in fact, was discovered by Bowman in the year 1841.

The degeneration consists in a transformation of the sarcous substance of the fibre into a hyaline structureless material which accumulates in irregular masses within the sarcolemma and distends it. Nothing is known of the chemical decomposition. The degeneration gives to the affected muscle a pale anæmic appearance, almost like fish-muscle (Zenker).

Mucoid or Myxomatous Degeneration (*μύξα, Mucus*).

136. **Definition.**—*A degeneration chiefly of connective tissues characterised by the transformation of the matrix into a jelly-like substance containing mucin.* In appearance the degenerated tissue much re-

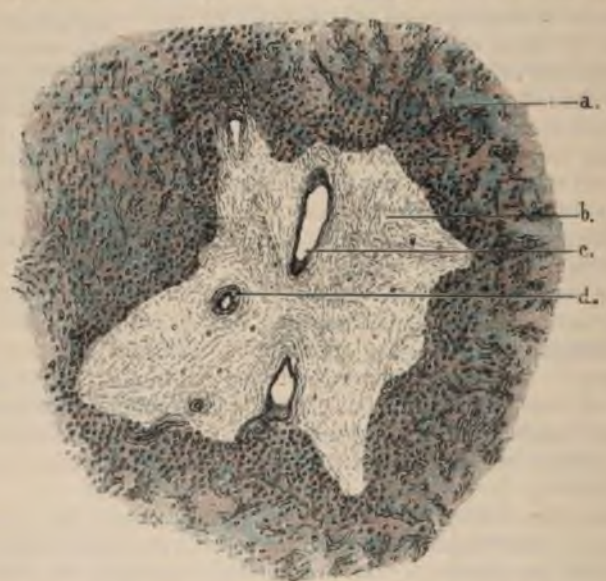

Fig. 63.—Mucoid Degeneration of a Sarcomatous Tumour showing a Myxomatous Space (×40 Diams.)

(*a*) Cells of the tumour; (*b*) myxomatous space; (*c*) a vein; (*d*) a small artery (Carmine).

sembles that affected by colloid, but has more of a trembling, jelly-like aspect. In the fœtus, at an early period of life, the whole of the subcutaneous areolar tissues consist of a texture highly loaded with this substance. The Wharton's jelly of the umbilical cord and the vitreous humour are both of a mucoid nature.

Pathologically, it is mainly a degeneration of connective tissue tumours, and may affect any of this group, such as the fibrous, sarcomatous, cartilaginous, or fatty. It is commonest in the sarcomata, and particularly in those of immediately subcutaneous origin.

General Characters.—The affected part has a peculiar gelatinous consistence. In the case of a myxomatous sarcoma, the tumour often projects in rounded masses, which, on being cut into, allow a quantity of semi-liquid ropy material to escape. The tumour is never equally affected by the degeneration, there being angular spaces within it in which the mucoid is chiefly contained. The intervening parts may present the ordinary appearances of a sarcoma.

Microscopically examined, the substance is quite homogeneous and perfectly transparent. It is seldom, if ever, that cells degenerate into it. On the contrary, they seem to grow readily within it, sometimes to huge dimensions, and throw out numerous branches. It thus differs from the colloid degeneration, in which the cells are the first element attacked. The intercellular substance is the part in which it first shows, and more particularly does it seem to select the adventitious coat of small arteries, along which it spreads so as to leave them dissected out in a transparent basis.

Chemical Nature.—It appears to be an albuminous complex, containing mucin in quantity.

Hyaline Degeneration.—Under this designation is described a peculiar glassy transformation which differs in certain respects from the wax-like, colloid, or myxomatous, although it seems to be closely related to the second of these. It chiefly affects lymphatic glands (Wieger, No. 13, lxxviii. 1879, p. 25, and Schüppel, No. 152) the vessels and neuroglia of the brain (Arndt, No. 13, xlix. 1870, p. 365), and the stroma of epithelial tumours (Malassez, No. 4, January, February, and March 1883). The part becomes infiltrated with a transparent homogeneous substance particularly within and around blood-vessels, which does not give the reactions of amyloid nor does it exhibit the histological characters of the mucoid. It differs from the colloid in being a degeneration chiefly of fibrous tissues. In the brain-cortex it sometimes forms extensive hard deposits producing a peculiar cartilage-like induration.

PIGMENTATION.

137. Most, if not all, natural pigments found within the body are derivatives of hæmoglobin, *i.e.* of the colouring matter of the blood. Certain pathological pigments are directly derived from different coloured secretions and excretions, but these primarily owe their origin to hæmoglobin.

Extraneous pigments find their way into the body from various sources.

The pathological pigments may therefore be classified as—

I. Those derived from the blood-colouring matter.

II. Those obtained from extraneous sources.

I. **Pigments derived from Hæmoglobin.**—(*a*) *Pigmentation due to hæmoglobin in solution.* After death the hæmoglobin readily

leaves the blood corpuscles and soaks into the tissues, giving them a pink, dark red, or livid colour, according to its amount. The best examples of this staining with hæmoglobin are to be seen in the endocardium and inner coat of the aorta when the blood has remained fluid after death. The staining must not be mistaken for congestion.

(*b*) *Hæmatoidin Pigmentation.*—The name "hæmatoidin" was given by Virchow to the pigment which is found in old hæmorrhages (No. 13, i. 1847, p. 383). When blood is extravasated and has lain in a tissue or cavity for several months or years, its colouring matter decomposes and becomes converted into this substance. It is common in aneurismal sacs and in old hæmorrhages into the brain.

It forms rhombic plates or rounded granules of a ruby or brick-red colour, and gives to the part in which it is contained an orange-red tint. It appears to be identical in composition with bilirubin ($C_{16}H_{18}N_2O_3$, Hoppe-Seyler), and does not contain iron. It further gives a play of colours with concentrated mineral acids.

(*c*) *Melanine pigmentation*, or *melanosis* as it is sometimes called, is the commonest variety. Melanine is the substance which gives the colour to various pigmented regions of the body, such as the uvea, choroid, and the rete Malpighii of the negro's skin.

Pathologically, it is chiefly a degeneration of connective tissue growths—sarcomata and fibrous tumours—especially such as grow from parts naturally pigmented. In Addison's disease the skin of the face, hands, neck, axillæ, nipples, front of the abdomen and external genitals, assumes a dark bronzed or mulatto colour from excessive pigmentary deposit. It is contained both in the rete Malpighii and in the fibrous derma, and assumes a granular form. In intermittent fever the spleen becomes highly melanotic, and the pigment particles are carried by the blood into neighbouring organs. The condition of the blood is known as *melanæmia*. It occasionally happens that where multiple pigmented sarcomata are scattered throughout the body the urine becomes coloured from the presence of melanine.

Unlike hæmatoidin, melanine is not a product of extravasated blood. It requires the action of living protoplasm for its elaboration. The cells concerned in its production elaborate it quite independently of any extravasation, and they are generally of a connective tissue type. It is questionable if the epithelial cells of cancerous tumours ever become truly melanotic—that is to say, assume a veritable melanine-forming propensity. The author has never seen such a tumour, and holds that if it does occur it must be rare. Blood extravasations take place into cancerous outgrowths, and the pigment may separate from these. This is something quite different, however, from a melanine-forming tumour. It is possible that, under certain circumstances, the connective tissue stroma of a cancer might become pigmented.

The percentage composition, according to Dressler, of melanine taken from a melanotic sarcoma was C51.73, H5, O7, N13.24 029.96,

Fig. 34. *Haematoidin Crystals from old haemorrhage into the brain. x 400 Diams.*

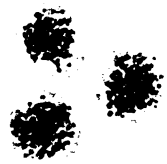

Fig. 35. *Haematoidin granules in liver cells, Cyanotic atrophy of liver x 400 Diams.*

Fig. 36. *Cells from a melanotic sarcoma. x 400 Diams.*

Fig. 37. *Entraneous pigmentation - Particles of coal & soot from a coal-miner's lung along with some pigmented catarr-hal cells. x 400 Diams.*

ash 1·47, but it seems to vary in composition according to the source from which it has been derived.

It is soluble in ether, alcohol, water, and acids. It is distinguished from black pigment of extraneous origin by being also freely soluble in boiling solution of potash, and by being decolorised when a stream of chlorine is passed through it. It does not crystallise, but remains in a granular form. *Microscopically examined*, it is seldom if ever black with transmitted light, a dark sepia colour being much more frequent. Extraneous black pigment, on the contrary, remains black even with high powers of the microscope.

(*d*) *Lutein Pigmentation.*—This is the colouring principle of the yolk of the egg and of the corpus luteum of the ovary. If not identical in composition with hæmatoidin, it is very closely related to it.

(*e*) *Bile Pigmentation.*—The chief colouring matter of human bile is bilirubin. When organs are accidentally stained with bile they assume a canary yellow, grass-green or olive-green colour. Gall-stones frequently contain large quantities of it.

II. **Pigments derived from Extraneous Sources.**—(*a*) *Pigmentation of Pus.*—Discharges from wounds, from the ear, and from other cavities, sometimes assume different colours. A pale azure blue colour is the commonest, but it may also be of a red, orange, green, or yellow tint. These colours are due to the development within the discharge of pigment secreting micro-organisms. The colour is contagious, and the particular organism can be cultivated on artificial media. Pyocyanin is the name given to the substance formed in the blue-coloured discharge.

(*b*) *Inhaled Pigment.*—From the atmosphere of ordinary dwellings and in following certain dusty avocations extraneous colouring matters are constantly liable to be inhaled and deposited in the lung. The lungs of all adults contain more or less black carbon particles from this cause. In coal-mining, enormous quantities of coal-dust and soot from lamps are inhaled, and give to the lung an absolutely coal-black colour.

The particles of coal or soot may be distinguished from true melanine by the following characters:—

(1) Microscopically, even with high powers, and when viewed with transmitted light, they are black, while melanine has seldom more than a sepia brown colour.

(2) The particles of coal are frequently spicular or in small irregularly-shaped scales. Melanine is always granular.

(3) The coal and carbon particles are insoluble in boiling potash, and are not bleached by chlorine, while melanine is readily soluble when boiled with potash, and is bleached by a stream of chlorine.

(4) Coal and carbon particles are not dissolved by sulphuric or hydrochloric acid.

(*c*) *Pigmentation from Silver.*—When a salt of silver is continuously administered for a lengthened period it causes a brown or black discoloration of the skin. The condition is known as *argyria*.

(*d*) *Metallic substances taken medicinally* into the alimentary canal, such as iron and bismuth, are liable to cause a black or slate-coloured precipitate in the mucous membrane of the stomach and intestine by becoming decomposed by sulphuretted hydrogen.

Coagulative Necrosis.

138. In the coagulation of the blood certain of the colourless corpuscles die and probably set free a ferment which, reacting upon the fibrinogen contained in the plasma, throws down a precipitate of fibrin. It has been said by Weigert (No. 13, lxxix. p. 87) that a similar ferment exists in the cells of the tissues. When they die, this ferment is liberated, and, under certain circumstances, precipitates fibrin in a finely granular form, causing the part to become hard and swollen, and very granular when examined microscopically. To this condition Cohnheim gave the name of **coagulative necrosis.** It follows more particularly where the circulation is suddenly arrested in a part, as in embolic infarction of the kidney and spleen.

Caseation.

139. **Definition.**—*Caseation is a dry fatty degeneration in which the albuminous and oily constituents of a tissue become converted into a substance like cheese in appearance, and somewhat allied to it in chemical composition.*

The term was invented for it by Virchow in the year 1852. Cheese of course contains an albuminous substance, casein, which is not found in this, but nevertheless there are other albumins present combined with fatty constituents, and the whole mass is dried and compressed into a cheese-like compound. The name, consequently, is by no means inapplicable.

Appearances.—When a part has fallen into this state it assumes a buff or cream-yellow colour, and becomes hard, sharply circumscribed, dry, and compressed. It is devoid of blood-vessels, and, when examined microscopically, has a peculiar, dusky, granular appearance, which readily demarcates it from the surrounding tissue elements. When the actual cellular and other constituents of the tissue are examined with a high magnifying power, they are seen to have become shrunken, shrivelled, dusky, and indefinite; and, finally, they break down into granular matter and very minute oil globules.

Tendency to Soften.—It is to be remembered that all caseous tissues are dead, and that any further degeneration which they may undergo is simply of the nature of a chemical decomposition probably induced by the presence of micro-organisms. The caseous mass often tends to soften in the centre, and the cause of this is apparently a chemical change by which the albumins of the part become converted into oil. The liquefied débris contains numerous free oil globules and

granular albuminous particles, with, frequently, shreds of elastic tissue. The process is probably analogous to the ripening of cheese. In course of time the débris is absorbed or otherwise got rid of, and a so-called *phthisical cavity* results. The cavity may heal by contraction, but if it be contaminated with the tubercle bacillus it is liable to induce a localised or wide-spread tubercular eruption. In this way an intractable tubercular disease arises, and in such cases the cavity remains open and continues to discharge broken-down caseous material from its walls.

Another method by which the caseous dead mass may be removed is seen in gummata and embolic infarctions. These are masses of caseous tissue which, instead of softening, become gradually absorbed

FIG. 64.—CASEATION IN A TUBERCLE OF THE LUNG (×350 DIAMS.)
(a) Reticulum of the tubercle; (b) granular caseous débris resulting from caseation of the same.

from the periphery inwards, evidently by the action of the surrounding lymphatics. Following upon this, a deep cicatrix results, often with a little calcareous nodule at its deepest limit.

Causes.—If the part which is about to become caseous is localised (*e.g.* a tubercule) the caseation invariably begins at its centre, and hence there is good reason for supposing that a diminished blood-supply is at least a cause powerfully predisposing to the degeneration. In some caseations, as embolic infarcts of the kidney and spleen, it is the sole cause. The drier the part, the more tendency there is to its occurrence. An œdematous lung, or one which contains much blood, seldom becomes caseous. Caseous pulmonary phthisis is a thing practically unknown in a person who suffers from regurgitant mitral disease—provided that the valvular lesion has been primary. It may be followed by a valvular lesion, but the order is seldom

reversed, the explanation, in all probability, being that the lung is so full of blood that the necessary conditions of malnutrition are not present to induce the degeneration.

Tubercles have a notorious tendency to caseate, and the cause is said to be the presence of the *tubercle bacillus*. It is a question as to whether the *syphilitic bacillus* may not also be the cause of the cheesy transformation of **gummata**.

In all persons having the **strumous diathesis** there is a great liability to the degeneration. Ordinary inflammatory deposits which would clear off in a robust person have a peculiar tendency to fall into a state of caseous necrosis in them.

CALCIFICATION.

140. **Definition.**—*The deposition within a tissue of insoluble compounds of lime and magnesia.*

The salts deposited are calcium phosphate ($Ca_3(Po_4)_2$), calcium carbonate ($CaCo_3$), calcium chloride ($CaCl_2$), calcium fluoride ($CaFl_2$), and magnesium phosphate ($Mg_3(Po_4)_2$) with occasionally traces of oxide of iron (Hoppe-Seyler, No. 30). They are thus identical with those found in bone.

Sites.—The cartilages of the ribs, the small arteries, the aorta in endarteriitis, and tumours of various kinds (myoma), are all tissues which are liable to calcification. Sometimes the minute arteries of the brain are so universally calcic that they stand out from the cut surface as fine bristle-like projections.

Appearances.—The calcic deposits give to the part a gritty feeling or a stone-like hardness. They are usually precipitated in the matrix of a tissue, but cases have been recorded in which nerve cells became entirely calcified (Förster and Virchow). The infiltrated part has a peculiar granular appearance when examined microscopically, which readily disappears with effervescence on addition of a mineral acid. The duskiness may be so great that the outline of the fibres among which salts are intercalated, is obscured. The granules are insoluble in alcohol and ether.

Causes.—Litten (No. 13, lxxxiii. p. 508) has shown that the process of calcification is intimately associated with coagulation of the albumin of a tissue. If the renal artery be ligatured in an animal, and the ligature removed after an hour and a half, so as to allow the circulation to return, the only change noticeable is an exudation of albumin into the Malpighian bodies. When the blood has continued to flow for twenty-four hours, however, this is followed by a precipitation of calcareous salts to such an extent that the organ may assume a stone-like hardness.

It is very liable to occur in old age, and Cohnheim explains this (No. 31, p. 528) by supposing that part of the dissolved phosphate of lime in the body exists in combination with albumin as a lime albuminate. In old age a quantity of albumin insufficient to combine with the entire lime salts is assimilated, and hence these become precipitated in the tissues. This is a mere conjecture.

Chalk Metastasis.—When a large tumour is situated in a bone, or when the

latter is the subject of softening, as from caries, calcareous deposits are liable to occur in other parts of the body. It is supposed by Virchow (No. 13, viii. 1855, p. 103) that the salts which are not required by the bone are thrown down in tissues which do not naturally precipitate them.

GANGRENE.

141. Fatty degeneration and caseation are both forms of tissue-death. Gangrene also implies that the tissue is dead. What is the difference between them?

Definition.—*Gangrene is the putrefactive fermentation of a dead limb or tissue still attached to the body.*

Many fatty or caseous tissues, although they are dead, may, and usually do exist in the body without putrefying, provided that they remain protected from putrefactive contamination. Internal organs, such as the spleen or kidney, do not become gangrenous when portions of them die, if they are not exposed to some source of organismal invasion. An *infarction* of the kidney or spleen is a dead but not a gangrenous tissue. It is caused by an aseptic embolus closing the channel of one of the branches of the splenic or renal artery. A *pyæmic slough* of these organs is a gangrene, and is caused by septic organisms being embolically carried into the vessels. In both cases the nourishment of the part is interfered with, but the result in the former is *coagulative necrosis* followed by caseation, in the latter a *gangrenous slough.*

Even where a dead part lies externally, as in a wound, it may slough without becoming gangrenous if precautions are taken to keep it aseptic. It constitutes an *aseptic slough* and separates from the living tissue by simple fatty degeneration. It has *decomposed*, but has not *putrefied.*

This leads to the definition of what is meant by decomposition and putrefication. **Decomposition** is a purely chemical process, such as the precipitation of the salts of iron in the blood by the sulphuretted hydrogen of the intestinal canal. **Putrefaction**, on the other hand, is a fermentation of the albumins of the part brought about by putrefactive organisms. A fœtus which dies *in utero* does not putrefy so long as the membranes are unbroken. It decomposes, however, and is converted, in course of time, into a substance like adipocere.

Appearances of a Gangrenous Part.—It becomes dusky red or purplish in colour by the transudation of the hæmoglobin from the blood corpuscles contained in it. Bullæ filled with fluid rise upon the surface; the part becomes swollen, and has a doughy or pulpy consistence; pain of a dull heavy character is experienced in it, and its temperature gradually sinks. This is followed by total loss of sensibility, and motion ceases. In course of time it becomes more or less greenish-black in hue; a peculiar and characteristic gangrenous odour is exhaled from it; a line of demarcation forms between the living and

the dead tissue, followed, in course of time, by a line of separation. Ultimately a complete separation of the one from the other ensues by a process of spontaneous amputation, the separated part being known as a *sphakelus*.

Microscopic Changes in the Tissue.—The blood is the first to undergo decomposition. Its colouring matter, as just said, is imbibed by the neighbouring tissues. The cells of the part are cloudy and granular; the muscular fibres disintegrate and become fatty; the white fibrous tissue swells and disappears; while the oil leaves the fat cells and becomes intermingled with the other tissues. The yellow elastic fibres seem to have more power of resistance than any of the other tissue elements.

The chemical changes essentially consist in the oxidation of the proximate principles composing the tissue, and ultimately culminate in the formation of carbonic acid, ammonia, and water. The other products are chiefly sulphuretted hydrogen, sulphuret of ammonia, valerianic, carbolic, and butyric acids, together with indol, skatol, etc. It is the combination of these which engenders the characteristic odour (see *Putrefaction*).

Certain crystalline products result from the process, and are found lying in the slough. They are chiefly leucine, tyrosine, margarine, and ammoniaco-magnesian phosphate, together with granules of sulphuret of iron.

The organisms found in it are those which are developed in liquids containing putrefying albumin—the organisms of putrefaction.

Causes.—In all cases the cause appears to be, primarily, either a complete deprivation of the blood supply, or an impairment of the nourishment by some other means; and, secondarily, the access of the organisms of putrefaction.

Literature on Degenerations.—Consult literature of various organs, and :—**Fitz** (Localised Amyloid): Boston Med. and Surg. Journ., cxiv. 1886, p. 389. **Genersich** (Amyloid): Pest. Med. Chir. Presse, xx. 1884, p. 1005. **Litten** (Amyloid): Deut. med. Wochnschr., xiii. 1887, p. 575. **Neumann** (Pigmentation): Arch. f. path. Anat., cxi. 1888, p. 25. **Nothnagel** (Compensatory Muscular Hypertrophy): Wien. Med. Bl., viii. 1885, p. 780. **Sutton** (Hypertrophy): Lancet, 1888, i. p. 61.

CHAPTER XII

INFLAMMATION

142. **Meaning of the Term.**—The word Inflammation literally means a burning (*inflammare*), and has been applied to designate the process on account of the subjective sensation of heat accompanying it. The term, however, simply refers to one of the cardinal symptoms of the disease; it does not inform us of what the morbid condition consists.

Can we therefore define succinctly, what is meant by inflammation? Most authors (*e.g.* Paget) have shrunk from attempting any narrow limitation of the term, mainly because the process is so complex. Sanderson (No. 52, vol. v., article "Inflammation") defines it as "*the succession of changes which occurs in a living tissue when it is injured, provided that the injury is not of such degree as at once to destroy its structure and vitality.*"

This is probably as comprehensive a statement as its varied phenomena will admit of. If we attempt any closer definition, difficulties arise on all sides. If it be admitted on the one hand that *cell multiplication* constitutes its essential factor, are we to conclude that a growing part is an inflamed part? Or, if it be granted that the *exudation of colourless corpuscles* from the blood-vessels takes place normally, how can we construct a theory of inflammation having this for its foundation? The process cannot be defined on either basis, for if we start with the hypothesis that inflammation is an exaggeration of either the one or the other of the above conditions, the question comes to be how much cell proliferation, or how much exudation goes to constitute it, and how much can be said to be normal. Where is the line of demarcation between them? Instead of having one code for the limitation of inflammation in all organs and tissues, it seems more reasonable to consider each upon its own special merits.

VASCULAR AND TISSUE CHANGES.

143. Two sets of phenomena are to be distinguished in the succession of changes to which injured tissues are subject, namely, those

occurring in the blood-vessels and their contents, and those which are found in the fixed tissue elements. By certain authors they are held to be disconnected and independent of each other. The whole tendency of modern investigation, however, seems to show that they proceed hand in hand. Even in tissues which are non-vascular or beyond the influence of the blood-vessels, such as the cornea, it comes to be a question whether in reality an alteration in the passage of the nutritive liquids through them be not the actual cause of the disturbance noticed in the fixed tissue elements.

It is often held that in a non-vascular part (cornea, cartilage) the process is a single one, that it is concerned exclusively with the fixed tissues; while in a vascular part it is of a twofold nature, and implicates both blood-vessels and fixed tissue cells. Seeing, however, that practically there is no tissue liable to become inflamed through which some kind of liquid does not circulate, and as this liquid is derived from the vessels and is subject to their alterations, such a view is somewhat short-sighted.

It will be more conducive, however, to a clear understanding of the process if we consider the two sets of phenomena separately, but before doing so it will be necessary to inquire into certain preliminary matters.

The Corpuscular Elements of the Blood.

144. Within the blood of all vivipara there are, at least, three, (Hayem) if not four, kinds of corpuscular element. The first is the ordinary coloured corpuscle; the second is the colourless corpuscle or leucocyte; and the third is what Hayem (No. 4, 1878, p. 692) calls a "hæmatoblast," and Bizzozero (No. 13, xc. 1882, p. 261) a "blood plate." Another corpuscle still is said to be present in blood, the so-called invisible corpuscle of Norris (No. 53), which, if it do exist, must not be confounded with either of the former.

Of the ordinary coloured corpuscles and leucocytes nothing further need be said at present, but as the hæmatoblasts appear to be bodies of very great significance in inflammatory and allied morbid states, some further notice of their morphological characters and physiological properties may be advisable.

THE HÆMATOBLASTS.

145. In the year 1865, Max Schultze (No. 14, i. 1865, p. 36) drew attention to the fact that there was a third corpuscular element in the blood, which he described as a small colourless sphere or granule. No doubt Beale in the foregoing year (No. 17, 1864) had drawn attention to a number of granules in the blood, which he called its germinal matter; but the account given of this granular or germinal matter by him renders it difficult to say whether the so-called granules corresponded to the "hæmatoblasts" of Hayem and "blood plates" of Bizzozero.

Granular matter has been described from time to time by different observers (Bettelheim, No. 54, xiii. ; Lostorfer, No. 55, 1872, p. 115 ; and Nedswetzki, No. 50, 1873, p. 147) as present in the blood in health and disease, to which an especial significance has been attached ; but there is good reason to believe that the granules so described were simply the result of disintegration of blood corpuscles or of hæmatoblasts during the act of coagulation. Riess (No. 51, 1872) and Laptschinsky (No. 50, 1874, p. 657) studied this granular matter in the blood of persons suffering from various diseases, and found that it was more abundant in some of them than in others. The former traced it to the destruction of the colourless corpuscles ; while Osler and Schäfer (No. 50, 1873, p. 577) regarded the granules as micro-organisms. It seems from recent observations that in all these cases, even although the blood had been examined almost immediately after being withdrawn, changes must have already occurred within it connected with coagulation which destroyed most of the hæmatoblasts, and from whose disintegration this granular matter resulted.

Hayem[1] undoubtedly was the first to give a clear account of this third corpuscle of the blood in his paper already referred to (1878). Bizzozero, whose chief work on the subject is contained in *Virchow's Archive* for the year 1882, simply corroborated Hayem's observations, the only point of importance in which he appears to differ from him being as regards the hæmatoblastic or blood corpuscle forming properties of these bodies. Hayem asserts that they are the germs of the future coloured blood corpuscles, and hence names them *hæmatoblasts.*[2] Bizzozero denies this, and calls them *blood plates.* There cannot be any doubt, however, that the bodies they refer to are alike.

Their rapid Destruction.—The reason of their not having been recognised before the above date rests in the fact that almost immediately after the blood is shed they undergo disintegration, so that by the time the blood has been withdrawn and prepared for examination, they have vanished, leaving nothing but a quantity of aggregated granules and fibrin threads in their place.

Methods.—In order to see them, they must be examined in the blood within a blood-vessel, or in blood which has been received in an apparatus capable of preventing coagulation. This object can be effected by cooling the slide and cover-glass down to about 0° C., but for their more complete study it is better to mix the blood with the accompanying fluid (Hayem) :—

Distilled water . . .	200	cc.
Sodic chloride . . .	1	grm.
Sodic sulphate . . .	5	,,
Mercury bichloride . . .	0·50	

This will preserve the coloured corpuscles and hæmatoblasts for something like 12 to 24 hours, and if the liquid be mixed with 10 cc. neutral glycerine, their natural

[1] Under the name of "Rothe Körnerkugel," Semmer (see ref. by Schmidt, No. 169, xi. p. 560) had referred to bodies which evidently are identical with Hayem's hæmatoblasts.

[2] Neumann employs the name "hæmatoblast" to designate the large nucleated blood-corpuscle forming cells found in bone marrow. These of course are quite different from the bodies under consideration.

diameter and appearances can be retained still longer. In drawing the blood a drop of the liquid should be put on the end of the finger (Laker). With a needle the finger is now pricked, and the blood allowed to mix with the liquor in the proportion of about 1 to 20 up to 1 to 100.

Affanassiew (No. 56, xxxv. 1884, p. 215) has used the undernoted mixture for the same purpose—

Distilled water . . .	100 cc.
Sodic chloride . . .	0·6 grm.
Peptone	0·6 ,,
Methyl violet . . .	1 per mille.

He says that it hinders coagulation, preserves the corpuscular elements, and renders their nuclei apparent.

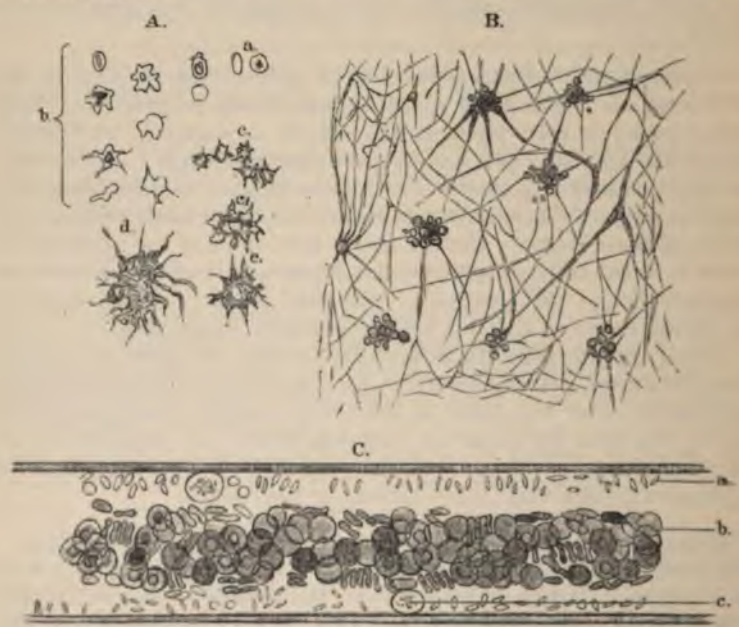

FIG. 65.

A. Hæmatoblasts (Hayem): (*a*) natural appearance when seen on surface and on edge; (*b*, *c*, c_1, *d*, and *e*) appearances presented by them during coagulation. B. shows the little heaps of granules formed by them after coagulation (Hayem). C. A small blood-vessel as stasis is approaching (Eberth and Schimmelbusch); (*a*) hæmatoblasts in peripheral stream; (*b*) coloured blood corpuscles; (*c*) a leucocyte.

Hayem (*loc. cit.* p. 710) recommends the following as the best means of studying the formation of fibrin from the hæmatoblasts:—Make, firstly, an ordinary slide preparation of blood, the edges of the cover-glass being dried with filter paper. Place the slide in a moist chamber and allow the blood to coagulate. Wash the colouring matter out of it by means of a stream of distilled water allowed to gradually run through the preparation from side to side, aided by the action of filter paper. Stain the reticulum of fibrin with saturated alcoholic solution of rose of Magdala, 1 part in 10 to 20 parts water.

Their Morphological Characteristics.—They are little, pale yellow coloured,[1] discoidal bodies, like faintly coloured blood corpuscles, and have a very delicate outline. The smallest of them are about 2 μ in diameter (1·80 μ), and from this they range up to 5 μ, the average size being 3 μ. It will thus be seen that they are considerably smaller than a coloured blood corpuscle (average, 7 to 8 μ). Hayem says that they have no nucleus, but as the result of an optical effect they may appear to be nucleated. They seem to possess a little stroma like the coloured blood corpuscles, and are evidently devoid of any cell membrane. They are equally abundant at all ages, from birth upward. Hayem calculates that they are forty times more numerous in Man than the leucocytes and twenty times less abundant than the coloured corpuscles. They become seriously altered in number in certain diseases.

Löwit (No. 12, xi. sec. iii. 1884, pp. 80-132) makes out that the hæmatoblasts or blood plates are simply masses of globulin (apparently para-globulin) which are extruded from the bodies of the leucocytes. He calls them consequently "globulin plates." He also asserts (No. 11, iii. No. vi. pp. 173-178) that, in the experiments of Schimmelbusch (Sect. 208), they were artificially generated in the circulating blood, owing to the salt solution in which the mesentery under examination was immersed. These views, however, have not met with acceptance, and it is generally recognised at the present day that the hæmatoblasts are natural constituents of circulating blood.

Their Influence in Coagulation.—Almost immediately after being withdrawn from the circulation they suffer the following changes, if means are not adopted to prevent coagulation (Fig. 65, A). They become, firstly, somewhat contracted, on which account their outline is rendered more striking, and they also appear more brilliant and shining. They next throw out around them a peculiarly viscous substance by means of which they tend to become attached to each other and aggregated into heaps. They are then suddenly transformed into little angular bodies, or they assume a stellate shape. If they are collected in a heap, the latter may take the form of a chaplet. From the border of these little masses or aggregations of transformed hæmatoblasts, fine, almost invisible, processes are projected into the surrounding plasma, possessed, to a certain extent, of the power of changing their position. Shortly afterwards throughout the whole field (Fig. 65, B) threads of fibrin are seen interlacing in all directions, and what remains of the group of hæmatoblasts seems to act as a centre from which these threads of fibrin radiate. After coagulation, the heaps of granules suffer comparatively little progressive alteration, further than that they lose their hæmoglobin, become totally decolorised, and, at the same time, are rendered more finely granular or homogeneous. Small vacuoles are occasionally met with in them, and little by little most of them ultimately suffer destruction.

[1] Bizzozero denies that they are coloured.

Influence in Wounds.—They thus apparently observe a most important purpose in bringing about the coagulation of the blood, evidently furnishing one of the elements (the fibrin ferment) necessary for its accomplishment. Where a wound is made in a tissue or vessel, the hæmatoblasts (Hayem, No. 40, xcv.) aggregate round its edges and apparently adhere to them. The fibrin is subsequently precipitated at the point where they are located, and, in this manner, they subserve the purpose of a natural hæmostatic.

They are also probably the means by which thrombosis is brought about within a living vessel (Eberth and Schimmelbusch, Hayem, and Bizzozero—see "Thrombosis").

NORRIS'S INVISIBLE CORPUSCLE.

146. Norris (No. 53) considers from his long continued investigation of the blood—(1) "That there exist in the blood of mammalia, in addition to the well-known red and white corpuscles, colourless, transparent, biconcave discs of the same size as the red ones; (2) between these two kinds of biconcave discs others having every *intermediate* gradation of colour are demonstrable." These corpuscles, judging from the description he gives of them as well as from his figures, are evidently quite different from Hayem's hæmatoblasts. He says that in ordinary blood they are invisible because their *colour and refractive index* coincide exactly with those of the liquor sanguinis. If the blood plasma be drawn off from the corpuscles they then come into view. Several ingenious methods of accomplishing this are described by him.

Mrs. E. Hart (No. 9, xxii. 1882, p. 255) believes that the Norris corpuscles do not exist in the blood as such, but that they are "unstable red corpuscles, or corpuscles of low resistance which have parted with their hæmoglobin possibly simply by the fact of the withdrawal of the serum." This authoress recommends the following very ingenious method of separating the plasma from the corpuscles, and so bringing the bodies in question into view. "A perfectly smooth and level slide is chosen, and at some slight distance from the centre a small hole is drilled, into which a metal eyelet is inserted, care being taken that the metal edge is not raised above the glass surface. A smooth and level thin cover-glass is now chosen and strapped on to the slide by means of a narrow piece of diachylon plaster so that the free edge exactly overlaps the metal eyelet; a screw fitting the eyelet is then inserted into the hole, and the method of procedure is as follows:—The tip of the finger is pricked and a drop of blood is placed, as rapidly as possible, at one of the free edges of the cover-glass; the blood enters by capillary attraction, forming a delicate even layer between the two glass surfaces; the slide is then inserted over a shallow vessel containing a 2 per cent solution of osmic acid, and the hinged cover-glass is gently raised by passing the screw further through the eyelet. All the fluid particles, and the great majority of the corpuscles, flow immediately towards the hinged edge of the cover-glass, leaving only a few red corpuscles, and here and there a white one, adhering to the glass surface; these are instantaneously fixed by the action of the osmic acid vapour." The cover-glass can be subsequently detached,

and the film of blood adhering to it or to the slide stained with a concentrated solution of nitrate of rosanilin in absolute alcohol. A drop of rosanilin is left for a few moments in contact with the corpuscles, and is subsequently washed off with distilled water.

The general conviction of continental and British (see Gibson No. 5, xx. 1886, p. 113) workers is in agreement with the above criticism, viz., that the Norris corpuscle is simply a coloured blood disc which has lost its hæmoglobin.

CHAPTER XIII

INFLAMMATION—(*Continued*)

On the Manner in which the Corpuscular Elements of the Blood Circulate.

147. Although it is a fact which has been familiar to every one from the time when the microscope was employed for the study of the blood circulation that the rapidity and nature of the movement of the coloured blood corpuscles differ materially from those of the colourless, still there has not yet been given a completely satisfactory explanation of the cause of these differences founded upon experimental data. It will therefore be expedient, firstly, to examine in how far these and other phenomena connected with the circulation of the blood corpuscles are subservient simply to the laws regulating the passage of bodies suspended in a liquid through a tube, and secondly to demonstrate how any interference with the natural position of the respective corpuscles in the vessels has a direct bearing upon inflammation and the circulation of the blood generally. The apparently trivial fact of the difference in the positions occupied by the two kinds of blood corpuscle has more importance than might be attached to it on superficial consideration, for, as will be shown in the sequel, if the coloured corpuscles did not occupy the centre of the stream, the circulation of the blood with the existing apparatus would become a physical impossibility.

NATURAL PHENOMENA—FROG'S WEB.

148. **Position Horizontal.**—The phenomena seen in the circulation of the blood corpuscles in a transparent membrane to which it is necessary to draw attention at present are:—

(1) There are two streams in the arteries and veins; the one axial and the more rapid, the other peripheral and the slower of the two.

(2) These streams are better seen in the arteries than in the veins.

(3) The coloured corpuscles and hæmatoblasts or blood plates float exclusively in the axial stream, while a great many, not all, of the leucocytes run in the peripheral.

(4) The number of leucocytes in the peripheral stream is greater in the veins than in the arteries.

(5) The motion of the coloured and colourless corpuscles differs, for while the former glide the latter rotate.

(6) In the veins the colourless have a tendency to stagnate when they get into the peripheral stream, the coloured have not.

(7) The capillaries have not any visible axial stream, and in those which admit a single corpuscle only, there is a tendency for the leucocytes more especially, but also for the coloured corpuscles, to stagnate.

149. **Position of Web Upright.**—These phenomena, however, have all been observed by examining the transparent parts of animals while they are in the horizontal position, the microscope being employed for looking at them from above downwards only. By this method of examination it is impossible to see whether the colourless corpuscles float in the peripheral layer all round the vessel, or only on the upper half of its circumference. It is also not easy to say from this mode of observation whether the coloured corpuscles float exclusively in an axial core, or whether some of them do not run along the lower border of the vessel. In order to look at the upper as well as the lower border of each vessel it is necessary to incline the microscope horizontally, and then to place the transparent part of the animal at right angles to it. In this way a clear view is obtained of all the strata of blood, and it can be seen exactly where each kind of corpuscle runs. The frog's web is perhaps best suited for the purpose.

If a large capillary vessel or small vein be selected for examination, it will be noticed that the coloured corpuscles float almost exclusively in the axial stream. It is a rare occurrence to find any of them in the upper or lower strata of the vessel. The most remarkable point in regard to this method of examination is in reference to the position of the colourless corpuscles. If a small vessel passing horizontally across the field be selected for examination, and if it run for a considerable distance without branching, it will be found that by far the greater proportion of leucocytes float on the *upper* surface, only a very small number on the lower. In the following table a series of observations made on different vessels of the frog's web is recorded. In all cases it will be seen that the proportional number of leucocytes found on what, in the position of the web, is the upper surface of the vessel, far outbalances that found on the lower. The observations were conducted on different vessels; some of them were almost straight, some had the convexity upwards, others downwards.

	Leucocytes passing along upper Surface.	Do. on lower.
Vessel No. 1. Convexity upwards . .	30	1
„ No. 2. Straight . . .	37	7
„ No. 3. Concavity upwards . .	57	10
„ No. 4. „ „ . .	8	0
„ No. 5. Convexity „ . . .	15	3
„ No. 6. Very short straight vessel .	16	3
„ No. 7. Convexity upwards . .	21	2

Indeed it seems only accidentally that a colourless corpuscle gets on to the lower surface of the blood stream, and, if carefully examined, this will be found to be accounted for in the following way:—[1]

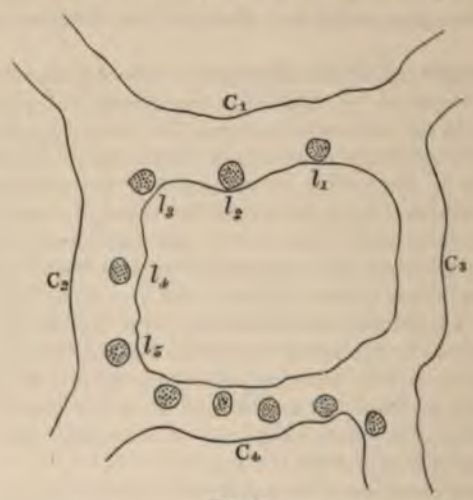

FIG. 66.

Let C_1, C_2, C_3, C_4 (Fig. 66) represent four large capillary stems, and let l_1 represent a leucocyte passing along the upper surface of capillary C_1. It continues to run towards C_4 in the direction of l_1, l_2, l_3, l_4, l_5, but when it enters C_4 it is now on the lower surface of the vessel, and the axial core of coloured corpuscles prevents it gaining the upper surface for some time. The coloured are in such mass that the comparatively small leucocyte takes some time to pass through them. Hence it runs for a certain distance on the lower border of the vessel. If it be watched for a sufficient time it can be seen ultimately to penetrate into the axial core of coloured corpuscles, and afterwards

[1] In looking at the web microscopically, of course, the positions are all reversed, the upper surface being the lower, and so forth. In the above scheme the parts are represented as they are actually seen, so that it will be understood that the surfaces are reversed.

to emerge on the upper surface of the vessel. Thus although the leucocyte may temporarily run along the bottom of the vessel it always tends, in the course of time, to gain the upper surface; so that if the number of leucocytes be counted on the upper and under surfaces of the vessel it will be found, as the above table shows, that by far the greater number pass in a given time along the *upper* surface.

When a capillary having a lumen sufficient to admit only one corpuscle at a time is observed, it is found that the leucocyte is pressed against the upper surface, and rolled along, while the coloured blood-corpuscle glides with much greater ease, and does not seem even here actually to touch the wall.

CAUSE OF THE PERIPHERAL AND AXIAL STREAMS.

150. There cannot of course be any doubt as to the cause of these. Water in moving in a canal proceeds in strata, the one stratum being pushed over the other. The stratum which is farthest away from the sides and bottom of the canal moves quickest. A tube is a double canal, and the central strata are subject to least friction, being furthest away from the sides. The strata in the axis therefore move quicker than those at the side. It is the friction between the side of the tube and the moving liquid which detracts from the velocity of the peripheral layers.

It is of importance to remember that the slower the stream passing through the tube the greater is the *absolute stagnation* in the peripheral area and the nearer to the centre are those strata which are moving with a given velocity, and which may be defined as "slow." The more rapid the stream (though the *relative* slowness of the peripheral strata is the same) the greater is the *absolute* velocity of the peripheral strata, and the nearer the wall of the tube is that stratum which moves at a given "slow" speed.

The coloured corpuscles float exclusively in the axial stream while a great many, not all, of the leucocytes run in the peripheral. The cause of this separation of the two kinds of blood corpuscle has been the subject of much speculation.

Thus it has been said that the colourless corpuscles are viscid, and that they tend to adhere to the side of the vessel. It has also been suggested that as they differ in size, it is this which causes the separation.

Donders (No. 144, Part V., 2d edition) explains it on the following basis:—The rapidity of the current increases towards the axis of the vessel; the spherical colourless corpuscle is applied with one side to this swift stream, the other being in the slower strata more towards the periphery. The corpuscle on this account does not make a continuous onward progress, but is revolved upon its axis, from which it is evident that it must be pressed out towards the periphery. The discoidal character of the coloured corpuscles, however, brings them always with their long diameter parallel to the axis of the vessel, and hence they tend to be driven onwards

in a given stratum without rotating. This explanation is also accepted by Cohnheim, but that it is erroneous the simplest experiment can demonstrate.

Foster (No. 145, p. 38) states the following:—"The corpuscles pass, where the friction is least, in the axis. A quite similar axial core is seen when any fine particles are driven in a stream of fluid through a narrow tube. The phenomena cease with the flow of the fluid. Many of the white corpuscles are frequently seen in the inert layer. This is said to be due to their being specifically lighter than the red corpuscles. When fine particles of two kinds, one lighter than the other, are driven through a narrow tube the heavier particles flow in the axis, and the lighter in the more peripheral portions of the stream. The white corpuscles, however, are distinctly more adhesive than the red, as is seen by the manner in which they become fixed to the glass slide and cover-slip when a drop of blood is mounted for microscopic examination: and by reason of this adhesiveness they may become temporarily attached to the walls of the vessel, and consequently appear in the inert layer."

Schklarewsky (No. 169, i. 1868, p. 671) writes:—"The blood is a fluid loaded with minute stable bodies. Mach and Bondy have long ago shown that by the addition of minute, insoluble, pulverised substances to a fluid the specific weight of the latter is raised. I can say in the special case of the blood that if it has stood for some time, the under half, which contains more blood corpuscles than the upper, also affects the araeometer distinctly more than the other, and, further, that it is specifically denser.

"Now if the lower strata of blood which is at rest are specifically denser through the accumulation of blood corpuscles, so, also, in circulating blood, the axial stream where the blood corpuscles press together, and where only the condensed hydrospheres fill the intervening spaces, will be specifically denser than the periphery. The specifically lighter white blood corpuscles will on this account in the normal circulation be pressed out into the less dense layers at the periphery."

That the ordinary phenomena noticeable in the circulation of the corpuscles are not due to any so-called vital action, but are purely physical in their effects, is proved by Schklarewsky's (*loc. cit.*) experiments on the passage of blood through a capillary glass tube. The same features are observed here as in the natural circulation. The author has repeated Schklarewsky's experiments, and is satisfied that the phenomena seen in the passage of blood corpuscles through the capillary tube are essentially the same as those noticed in their circulation through the natural blood channels. Seeing, therefore, that the wall of the vessel, the heart, vasomotor nerves, and other parts of the circulating apparatus are unnecessary for the production of the phenomena just enumerated, it follows that their explanation is to be sought in the study of those forces which influence bodies suspended in a liquid circulating through a tube.

Experiments on the Circulation of Bodies through Large Tubes.

151. A capillary tube, from its small size, and from the fact that only one side can be observed at once, is inconvenient for studying the conditions under which bodies float in different parts of the stream. The following experiments show that the laws which influence the

passage of *solid bodies suspended in a liquid* through capillary tubes are the same as those which guide them in their transit through tubes of larger size, provided that the proportional dimensions between tube and bodies circulated be maintained. It is therefore evident that if we employ a tube and circulating bodies of large size in addition to capillary tubes we can make experiments with a nearer approach to accuracy than if we employ capillary tubes alone with circulating bodies correspondingly small. By subsequent comparison, it will be found that the same conditions hold good for both.

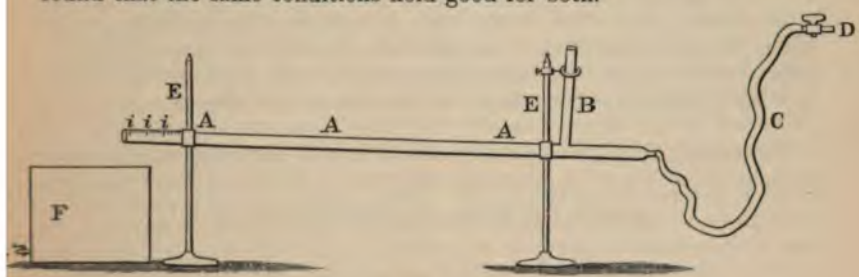

FIG. 67.

The apparatus for these experiments has the following construction :—A, A, A (Fig. 67) is a glass tube 6 ft. long and having a bore of 1 in. At one end it is attached to an india-rubber tube C, which communicates with a water-cistern by the stop-cock D. The water entering at C runs through the tube into a tank F which has an escape pipe G. At a distance of 5 ft. 5 in. from the distal end a second tube (B) is cemented at right angles, and through this, bodies can be introduced into the circulating stream.

The whole apparatus is supported upon two uprights E, E.

In order to keep the tube full, or nearly so, when the water is circulating, it is elevated about ¾ in. at the distal extremity. The cistern is most convenient when placed at a height of about six feet. When about to be used, the circulation of the liquid is first allowed to become thoroughly stable ; all air must be driven out ; and the strength and pressure of the stream may be recorded by an index at the distal end of the tube (*i*, *i*, *i*). In this way, with the same elevation of the end of the tube, we can easily ensure a uniform strength and velocity of the current.

The first series of the present experiments consists in the introduction of solid bodies of various weights, sizes, shape, and specific gravity. For a long time the author employed bodies made of gelatine and variously coloured so that they might be easily distinguished. After having a little experience of these, however, it was found that the results obtained by their use were not trustworthy, owing to their being capable of absorbing water. There is also another inconvenience connected with them, namely, that they get soft when kept for any time, and are hence rendered unserviceable. These deficiencies can all be got over by substituting bodies made of white wax instead of gelatine. This can be mixed with various pigments in powder so as practically to render them of any required specific gravity, and at the same time to give each a distinctive colour. Brunswick green and vermilion will be found very useful for mixing, but any other heavy pigments may be employed in the same way. The wax should first be melted, the pigment being subsequently mixed with it while warm. If the bodies, after being made, are slightly lighter than what is required,

this may be corrected by rubbing into them, in the palm of the hand, a little of the pigment. The warmth of the hand is sufficient to cause the pigment to adhere to the wax. It need hardly be added that before comparing the specific weight the wax should be allowed to cool.

In order to make spheres, a bullet mould should be employed, and for discs, the wax should be poured out, when melted, in a layer of uniform thickness, discs of various sizes being then punched out of it with cork-cutters. Bees' wax being such a plastic substance, bodies of any other shape may easily be devised.

In the first set of experiments the stream, in strength and velocity, must remain the same throughout, the most suitable fixed points being the before-mentioned elevation of the tube to $\frac{3}{4}$ in., with the water level at $6\frac{1}{4}$ in. from the distal end. It will be expressly stated in what experiments the velocity of the stream was altered.

EXPERIMENT No. 1.—*Four spheres made with the same mixture of wax, Brunswick green, and vermilion, and so specifically heavy that they readily sink in water.*

Sphere	$a = \frac{7}{8}$th	inch in diam.	and weighs	90	grs.
,,	$b = \frac{3}{4}$	,,	,,	65	,,
,,	$c = \frac{3}{8}$	,,	,,	15	,,
,,	$d = \frac{1}{8}$	,,	,,	2	,,

They may be dropped into the tube separately or together without making any difference in their relative rapidity of motion.

Sphere *a* (which was almost equal in diameter to the bore of the tube) went through with the above given stream in $11\frac{1}{2}$ seconds.

Sphere	*b*	went through	in 12	secs.
,,	*c*	,,	,, 15	,,
,,	*d*	,,	,, 17	,,

It was noticed that they all rested on the lowest part of the tube. It was further observed that they all had a rotating motion.

We may therefore conclude that *with spherical bodies whose specific gravity is equal, but considerably greater than the suspending liquid, the larger the body is, provided it does not quite fill the tube, the quicker it moves.* This experiment also shows that, *ceteris paribus*, so long as the spherical shape is retained, the heavier body (actual weight) also circulates much *quicker* than the lighter, for notwithstanding that the heaviest of the four balls weighed 90 grs. while the smallest weighed only 2 grs., yet the rate of circulation in the case of the former was much greater than in that of the latter. It shows further, that they all rotate even when the body fits almost accurately into the tube. In the above case, the largest sphere did not exactly fill the tube, the smallest perceptible space being left at the upper level.

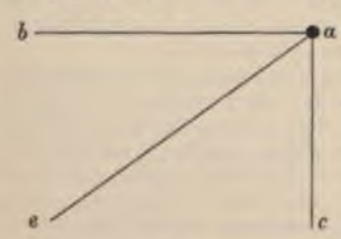

FIG. 68.

The explanation of these phenomena is very simple:—When a body, of any shape or size, is introduced into such a stream, there are mainly two forces which come to act upon it. Suppose *a* (Fig. 68) represents one of the four balls which is introduced into the tube. Immediately after it enters the water, it tends, on the one hand, to be carried forward by the moving strata of liquid, while it also tends to be carried downwards by its specific gravity. And if we suppose these two forces to be represented respectively in magnitude and direction by the lines *ab*, *ac* (Fig. 68), then the position occupied by the body in the circulating stream will be at *e* in the direction *be*. But being intercepted by the tube, and the horizontal force being continuous, it will then move along its lowest border. The specific gravity in the above case was so much greater than the force represented by the stream, that the body almost immediately came to the bottom of the tube.

Why is it, however, that the larger body should move through the tube with so much greater velocity? The reason is also apparent. The larger body gets more of the swift and powerful axial strata than the smaller which lies at the bottom of the tube. It is therefore impelled forwards with greater rapidity than the smaller which is kept running in the part of the tube where the strata of liquid move slowest.

The spheres all have a rotatory motion. The cause of this is that the one side of the sphere, that which is nearest the axis of the tube, is subjected to the action of the swift strata, that which is further away lies in the slow strata and is pressed against the tube wall. The inevitable consequence is that the ball is rolled over and over round its axis. So long as the specific gravity of the body is markedly greater as a force than the onward current, the rolling of the sphere into the axis of the stream can never happen.

Even the largest ball rotates, the reason being that it does not exactly fit the tube. The ball rests more against the lower aspect of the tube than the upper, and hence the friction on the lower side is greater than that on the upper.

It will continue to rotate until the friction is equalised on all its sides. If one side, any side, of the sphere touches the tube it will rotate. If, on the contrary, as we shall afterwards see, the circumference of the sphere is not in contact with the tube at any point, rotation does not take place.

EXPERIMENT No. 2.—*Spheres made of spermaceti of same size as those in No. 1. Stream as before.*

$a=\frac{1}{2}$	in.	diam.,	weighs 69	grs.,	passed	through the tube	in upper stream	in 12 secs.
$b=\frac{3}{8}$	,,	,,	48	,,	,,	,,	,,	$12\frac{1}{2}$,,
$c=\frac{3}{4}$	,,	,,	4	,,	,,	,,	,,	13 ,,
$d=\frac{1}{8}$	,,	,,	$\frac{1}{2}$ gr.	,,	,,	,,	,,	$13\frac{1}{2}$,,

They all have a rolling motion, and pass through the tube in the same order as in Experiment No. 1.

We may therefore conclude, that *with spherical bodies whose specific gravity is less than the suspending liquid, the larger the body is, provided it does not quite fill the tube, the quicker it moves.* It also follows, that *if a sphere is specifically lighter than the liquid in which it is suspended, it will sooner or later come to occupy the upper strata, and will rotate.* It will pass to the periphery and rotate for the same reasons as those which influence the body of heavy specific gravity. One side, the upper in this case, comes in contact with the tube, the opposite side being impinged upon by the swift filaments of liquid.

EXPERIMENT No. 3.—*Spheres of specific gravity as nearly as possible equal to that of water.* They should be made of wax and Brunswick green and be of the same size as those employed in Experiments 1 and 2.

$a = \frac{7}{8}$	inch diam.,	weighed	78 grs.,	passed	through	tube in	$11\frac{1}{2}$	secs.
$b = \frac{5}{8}$	,,	,,	50	,,	,,	,,	11	,,
$c = \frac{3}{8}$	,,	,,	5	,,	,,	,,	$9\frac{1}{2}$	,,
$d = \frac{1}{8}$	,,	,,	1 gr.	,,	,,	,,	$9\frac{1}{2}$	,,

They do not rotate, but *have a smooth gliding motion.* They all keep, as far as their size admits, the axial stream. Even the largest does not sufficiently impinge against the sides of the tube to cause any rotation; there is a minute space between the tube wall and the surface of the sphere all round. The smallest spheres occasionally touch the bottom of the tube shortly after starting, but are again almost immediately drawn into the axial current, and pass through the greater length of the tube within this. Out of a number of spheres of the same size, if there is one which approaches nearer to the actual specific gravity of the water than the others, that sphere keeps in the axial stream most steadily.

The indications from this experiment are very important. It clearly shows, that, if a body is to run in the axial current, it must be as nearly as possible of the same specific gravity as the liquid in which

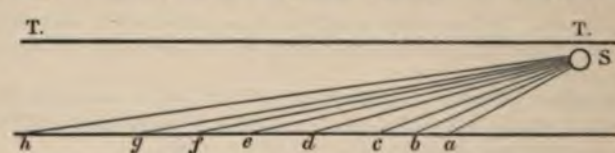

FIG. 69.

it is suspended. *The nearer the suspended body approaches to the specific weight of the liquid in which it is immersed, the more it tends to occupy the centre of the stream.*[1] The cause of this is apparent when we construct a diagram as before. In all the previous experiments there were practically two forces at work on the immersed sphere. The one, its specific gravity, tending to pull it downwards or upwards, as the case may be, the other, the current, tending to drive it onwards. As previously shown, the situation ultimately assumed by the immersed body corresponds to the resultant between the two.

Let TT (Fig. 69) be the tube and S the sphere immersed in the water circulating through it. It will be apparent that, according to the relationship of the specific gravity of the sphere to the water in which it is immersed, the course which the former will pursue will be more or less oblique. If the horizontal force be not much greater than that corresponding to the specific gravity, then the diagonal would be represented by line S*a* or S*b*. But if the disparity is much greater,

[1] Eberth and Schimmelbusch are certainly in error when they state (No. 13, cv. 1886 p. 464) that "a stream of fluid in a tube is always more rapid in the axis than at the wall, and that corpuscular elements, heavier than the fluid and mixed with it, are drawn into this swift axial area."

then the course which the sphere will pursue will be more oblique, as in S*g* or S*h*.

It therefore follows, that the nearer the specific gravity of the suspended body approaches to that of the liquid in which it is held, the more oblique will the diagonals become, that is to say, the directions followed by the various bodies will be such as those represented in Fig. 69 by S—*a*, *b*, *c*, *d*, *e*, *f*, *g*, *h*. If, however, the body is of exactly the same specific gravity as the liquid in which it is suspended, there is of course no downward or upward force, but, being bulk for bulk equal with the water, it is simply impelled onwards as part of the circulating liquid. Under such circumstances the suspended body always tends to get into the axial current.[1]

If some of the spheres in this experiment are accidentally a little heavier than water, they tend from time to time to get out of the axial stream. They rebound, however, the moment they touch the tube, and fall again into the axis. The same thing is noticed if they are *slightly lighter* than water. There is a certain small limit within which a body may be specifically lighter or heavier than the liquid in which it is suspended and still practically retain its axial position. With small differences in specific gravity the diagonal is so oblique as to be almost imperceptible in its inclination from the horizontal.

The above experiment, however, also demonstrates that *if the specific gravity of several different sized spheres is equal to that of the liquid in which they are suspended, the larger the sphere, the slower it circulates.* In

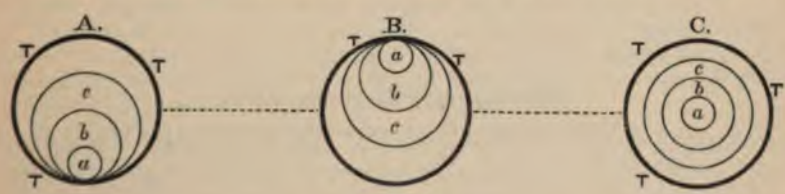

FIG. 70.

Experiments 1 and 2, where the different sized spheres were of heavier or lighter specific gravity than water, exactly the reverse of this was found to be true. In these cases the larger the sphere, the quicker it circulated.

The cause of this is explained in Fig. 70. Let T in A, B, and C represent sections of the tube. So long as the spheres (*a*, *b*, *c*) do not fill the tube, A would represent the position of those which are heavier than water, and B that of those which are lighter. Now it is evident that both in A and B *the larger the sphere up to a certain limit in which it nearly fills the tube, the faster it will move*, because it receives more relatively of the swift filaments than one which is smaller. It can

[1] The author will not attempt to explain why this is so; the problem of the manner in which a particle of liquid moves through a tube is so complex as to have baffled many of our most accomplished physicists.

touch the tube only at one point, and hence escapes the action of the greater number of the slow filaments lying close to the tube wall.

Spheres, however, of the same specific gravity as the water, as before said, float in the centre of the stream. Fig. C would, therefore, represent their position, and it now becomes plain that in this case *the smaller the sphere the more of the swift and the less of the slow filaments will impinge upon it, and hence the faster it will circulate.*

It is to be observed, however, that when a certain minimum of size is reached, where the body is of the same specific gravity as the liquid, the rate of progress does not appreciably alter, showing that in a moderately rapid stream the central filaments circulate practically with almost equal velocity.

The experiments (Nos. 1, 2, and 3) just quoted, show some other interesting points as regards the relative rate of transmission of spheres heavier, lighter, and of the same specific gravity as the liquid in which they are suspended. The results obtained are the following—

Spheres of heavier specific gravity than water.

$a=\frac{7}{8}$	inch	diam. and	weighs 90	grs.,	passes through in	11½	secs.
$b=\frac{5}{8}$	,,	,,	65	,,	,,	12	,,
$c=\frac{3}{8}$	,,	,,	15	,,	,,	15	,,
$d=\frac{1}{8}$	,,	,,	2	,,	,,	17	,,

Spheres of lighter specific gravity than water.

$a=\frac{7}{8}$	inch	diam. and	weighs 69	grs.,	passes through in	12	secs.
$b=\frac{5}{8}$	,,	,,	48	,,	,,	12½	,,
$c=\frac{3}{8}$	,,	,,	4	,,	,,	13	,,
$d=\frac{1}{8}$	,,	,,	½ gr.	,,	,,	13½	,,

Spheres of same specific gravity as water.

$a=\frac{7}{8}$	inch	diam.,	weighed 78	grs.,	passed through tube in	11½	secs.
$b=\frac{5}{8}$	,,	,,	50	,,	,, ,,	11	,,
$c=\frac{3}{8}$	,,	,,	5	,,	,, ,,	9½	,,
$d=\frac{1}{8}$	,,	,,	1 gr.	,,	,, ,,	9½	,,

It is apparent from this comparison that, notwithstanding differences in size, in no case did the specifically heavy or light spheres go through in less time than those which were of specific gravity equal to the water.

We may therefore conclude that *a sphere whose specific gravity is the same as the suspending liquid will circulate faster than any similar sphere of different specific gravity.*

EXPERIMENT No. 4.—*Three spheres of equal size but of different weight, and all much heavier than water.* Stream as before. They may be made of wax and vermilion, the latter added in different quantity to each. Each may be ⅞ inch in diameter, and the only material difference between them is in regard to their weight.

They should be started in the tube at exactly the same time, and should at first be in apposition. The one of lowest specific gravity is placed in front, that of medium specific gravity second, and that which is heaviest last. By the time they

reach the end of the tube, the first will be found far in advance of the second, and the second before the third, the distance of separation depending on the disparity in their weight.

The conclusion from this is, that *with spheres of the same size and of greater specific gravity than the suspending liquid, the heavier the body the slower it moves.*

EXPERIMENT No. 5.—*Two spheres, one made of spermaceti, the other made of cork covered by spermaceti, and both of the same size,* the cork sphere being considerably the lighter of the two.

Both have a rotatory motion, and the spermaceti sphere moves much the faster of the two.

It is, therefore, evident that with spheres of the same size and of less specific gravity than the suspending liquid, the lighter the body, the slower it moves.

Comparing experiments 4 and 5 we may also conclude that, other things equal, *the greater the divergence in either direction of the specific gravity of the suspended bodies from that of the liquid in which they are immersed, the slower they circulate.*

EXPERIMENT No. 6.—*Bodies of different shapes, of the same absolute weight, and of like specific gravity as water.*

For this experiment take a disc and a sphere made of wax so mixed with vermilion as to be of equal specific gravity with water. The sphere may weigh 5 grains and be $\frac{1}{4}$ inch in diameter; the disc must have the same weight and diameter; the only difference between them is as regards their shape.

They pass through the tube in exactly the same time, one sometimes getting in front of the other at first, but ultimately settling down to a definite position in the axial current, and moving with exactly the same rapidity. The time occupied is from 9 to 10 seconds. They both have a gliding motion.

The conclusion from this is, *that a disc and a sphere of the same specific gravity as the liquid in which they are immersed, and differing only as regards their shape, move with the same rapidity and do not rotate.*

EXPERIMENT No. 7.—*Bodies of different shapes, of the same specific gravity as water, but differing in absolute weight.*

Take a cylinder $1\frac{1}{4}$ inch long and $\frac{3}{8}$ inch broad made of the same material as in the foregoing experiment, and a disc $\frac{1}{10}$ inch thick cut from the end. Both circulate in the same time and both have a gliding motion. Any other shape may be substituted, provided it does not bring the one body in contact with more or with different filaments of liquid than the other.

From this we therefore learn that *bodies of different shapes and absolute weights, but all composed of a material of like specific gravity as the liquid, circulate in an equal time, provided they are so constructed as to float in the same part of the current.*

The reason is, of course, that being of the same specific gravity as the water they simply displace an equivalent bulk of it and move as part of the general stream, so that if, from their size and shape, they come in contact with the same strata they will move at the mean rate of these strata.

An important point to remember, however, in these experiments, to avoid fallacy, is that the bodies must be of such an actual weight that their inertia will keep them steadily in the same part of the tube. Although a very thin disc, for instance, will, if it remain in its proper stratum, go through in the above manner, yet, if very light, it tends to be displaced by rebounding against the tube more than a mass of greater size and having greater inertia. A fallacious result is very apt to enter into experiments, if this be not attended to.

EXPERIMENT No. 8.—*A disc and a sphere of the same material, diameter, and absolute weight, but both of greater or less specific gravity than water.*

Take a disc made of wax and vermilion much heavier than water and a sphere of the same material both ½ inch diameter. Let the thickness of the disc be ⅛ inch. Pass them through the tube with the stream as before. If the disc roll on its edge, which it has a great inclination to do, it will pass through the tube in the same time as the sphere. If however, as sometimes happens, it lies horizontally in the tube it will go much slower than the sphere.

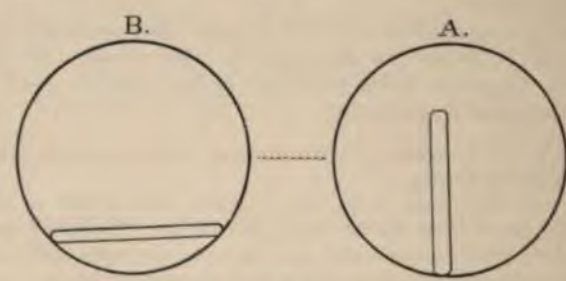

FIG. 71.

So long as the disc is on edge, it rolls like the sphere, as in Fig. 71 A., but if it falls so as to lie horizontally (Fig. 71 B), then, as may be perceived, its circumference rests on the tube at two sides and it floats along in a single stratum without rotating, that stratum being near the bottom of the tube, and, consequently, very slow in its rate of progress. The same holds good for discs of lighter specific gravity than the suspending liquid, the only difference being, of course, that they seek the upper instead of the lower level of the tube.

In other respects, if they rotate on their edge, they behave exactly like spheres.

The conclusion from this is, that *a disc specifically heavier or lighter than the suspending liquid behaves like a sphere of the same absolute weight, material, and diameter, in its passage through a tube, provided it runs upon its edge.*

152. **Conclusions from preceding Experiments.**—Putting the facts we have obtained from these experiments together, we arrive at the following conclusions so far as regards a tube with a wide bore.

1. With spherical bodies composed of the same substance whose specific gravity is either lighter or heavier than the suspending liquid, the larger the body is, provided it does not quite fill the tube, the quicker it will circulate.

2. With spherical bodies composed of the same substance whose

specific gravity is identical with the suspending liquid, the smaller the body, the quicker it will circulate.

3. The only body which will circulate in the axial stream is one whose specific gravity is identical with, or approaches, that of the suspending liquid.

4. A body of any shape which will float in the axial stream has a gliding motion; all others tend to rotate from the friction caused by rubbing against the tube.

5. A sphere of any size, provided it does not fill or nearly fill the tube, and of the same specific gravity as the suspending liquid, will circulate faster than a similar sphere of any other specific gravity.

6. Other factors being alike, the greater the divergence in either direction of the specific gravity of the suspended bodies from that of the liquid in which they are immersed, the slower they circulate.

7. The shape of bodies does not materially alter their rate of progress, provided they are so constructed as to be influenced by the same filaments of liquid and to rotate.

The Phenomena of the Circulation in the Ultimate Capillaries Considered in the Light of the Foregoing and Similar Experiments.

153. The circulation in the ultimate capillaries, that is to say, in those which admit no more than a single row of blood corpuscles, is characterised by the following phenomena:—

(A) There is not, of course, any axial core of coloured corpuscles.

(B) The coloured corpuscles glide, the colourless roll, even in an animal with round coloured corpuscles, and both circulate with nearly equal rapidity.

(C) The circulation within the vessels sometimes ceases by a colourless corpuscle blocking the tube, even although it may be smaller than the coloured.

Let us examine and endeavour to explain these phenomena in the above order.

(A) In a capillary tube of moderate dimensions there appears to be an axial stream of liquid just as in a larger tube, but the corpuscles being too large to occupy this exclusively, the axial core is, of course, absent. The relationship, therefore, comes to be very much the same as in the apparatus previously described when we employ bodies of such size as to correspond in relative dimensions with the corpuscles in an ultimate capillary.

(B) Experiment No. 9.—*Large tube as before. Three spheres nearly filling the tube.* Same stream.

(*a*)	*Specifically heavier than water*	Rotates.	Time = 11½ secs.
(*b*)	,, *lighter* ,, ,,	Rotates.	,, = 12 ,,
(*c*)	,, *the same as* ,,	Glides.	,, = 11½ ,,

EXPERIMENT No. 10.—*A sphere and a disc both of same specific gravity as water and both nearly filling the tube.* Both pass through the tube in 11½ secs. and both glide.

Starting upon the assumption that the colourless corpuscles are specifically the lighter of the two, the coloured approaching nearer to the specific gravity of the plasma, we have, in the above experiments, a complete explanation of the rolling and gliding motions. The specifically light corpuscle comes in contact with the vessel wall more than that which is of the same specific gravity as the plasma, and hence, as before explained, will roll. The fact that the colourless roll in an ultimate capillary while the coloured, even when of round shape, glide, is strong proof of their difference in specific gravity and of the nearer approach of the specific gravity of the coloured to the blood-plasma than that of the colourless.

Another curious point as regards the ultimate capillary circulation is, that there is no marked difference in the rapidity of motion of the two kinds of corpuscle. As will be seen from Experiments 9 and 10, this is fully borne out, for when we come to bodies of different specific gravity nearly filling a tube the difference in the rapidity of their motion becomes infinitely less than when they are smaller. From the above results it will be seen that it was only half a second in a distance of 5½ feet. The reason for this, in all likelihood, is, that when the circulating body is so large as almost to fill the bore of the tube the amount of space between its circumference and the interior of the tube is so slight that no great amount of water can pass between them. Each sphere therefore receives nearly the full force of the entire stream, so that it is impelled onwards quite irrespective of the comparatively slight resistance caused by their greater or less friction.

(C) The cause of a colourless corpuscle blocking the tube undoubtedly is that its light specific gravity tends to press it upwards against the wall of the vessel, to which it may even become temporarily adherent.

154. **Lessons from above.**—From these experiments we learn that if the coloured corpuscles were not so balanced as to closely approach the specific gravity of the plasma, the circulation of the blood would become a physical impossibility; for if they were markedly lighter or heavier than the plasma, they would constantly tend to obstruct the capillaries and to hinder the onward flow. The essence of the blood as a circulating fluid is that the large majority of the corpuscles never touch the wall of the vessel, but glide in the central stream. Were the coloured corpuscles to rub against the wall of the vessel, the friction would be so enormous over the whole capillary system that the heart, as at present constituted, would be wholly inadequate to drive the blood onwards. Indeed it is possible that if the blood corpuscles all differed materially from the specific gravity of the plasma, the circulation could not be carried on under any circumstances.

Some time since it was proposed by surgeons to **transfuse milk instead of blood** in cases of traumatic or idiopathic anæmia. In all cases, however, so far as the author has examined into the subject, the symptoms which have followed the injection of milk into a vein have been of the most alarming character. Miglioranza (No. 57, 1883, and No. 49, p. 249, 1883) found that milk introduced into the circulation of dogs caused dyspnœa, vomiting, diarrhœa, prostration, and even death.

Milk serum alone had no effect. Difficulty of breathing and lividity of the face constantly accompany this procedure in Man, when the quantity of milk transfused has been at all large. The transfusion of milk has accordingly fallen into disrepute for this reason. Most of the milk globules from their light specific gravity would be sure to float into the peripheral layer on the surface of the blood stream, and would pass through the pulmonary capillaries with the greatest difficulty. This is the explanation of the dyspnœa.

Another example of the same thing is seen in **fat embolism** from fracture of a bone, and in the **lipæmia** of diabetes where the blood contains a great quantity of a fatty emulsion. Under such circumstances the impediment to the circulation results, in the course of time, in a total arrest of the blood stream.

Air embolism, where for instance air is aspirated into a vein in a surgical operation, proves fatal from a like cause. The air globules are much too light to circulate and they form embolic obstructions.

The foregoing facts demonstrate the exquisite adaptability of the blood for circulating purposes, and also show the great danger of allowing substances of wrong specific gravity to enter the blood-vessels.

Experiments on the Circulation of Bodies through Capillary Tubes.

155. In most respects the author has found that the **circulation of bodies through capillary tubes** is regulated by the same laws as the circulation of larger bodies through correspondingly larger tubes, such as those employed in the foregoing experiments. In order to see the exact part of the capillary tube occupied by bodies circulating in it, it is necessary to place it horizontally, with the microscope similarly inclined. Looking at the tube from above, it is impossible to see the different layers of liquid and the bodies contained in them with exactitude.

The capillary tube ought to be cemented to a slide with glycerine jelly and covered with a glass slip. It is attached at one end to an aspirating bottle, and, at the other, is placed in the liquid to be circulated. In all cases special care must be taken that the bodies suspended in the liquid are sufficiently small to enter the capillary tube. In order to ensure this it is necessary to filter the liquid in all cases through muslin or some such coarsely porous substance.

Experiment No. 11.—*Circulation of blood through a capillary tube.*

The capillary tube apparatus having been all previously arranged, the head of a water newt or frog is cut off and a few drops of blood allowed to fall on a watch-glass previously cooled. This is immediately brought in contact with the end of the capillary tube and must be looked at microscopically very soon after reaching the part of the tube under the microscope, otherwise the coagulation which occurs will put a stop to its passage. When looked at in the horizontal position as before described there is seen to be a clear area on the upper surface of the tube[1] in which *exclusively* the colourless corpuscles run. Not a single colourless corpuscle is to be

[1] The positions are of course reversed. In all his remarks the author refers to *the actual* upper surface, that is to say, the lower surface as seen microscopically.

seen on the lower surface of the tube. The coloured corpuscles occupy the axial stream as in the circulation through the blood-vessels. If after coagulation has occurred, and after the transmission of the blood has consequently ceased, the capillary tube be moved along under the microscope, the colourless corpuscles will be still found on the upper surface. It should also be mentioned that the leucocytes here, as in the vessels, have a rolling motion, while the coloured blood corpuscles glide.

EXPERIMENT No. 12.—*Blood which has been defibrinated and whose specific gravity is* 1040.

This runs comparatively easily through a capillary tube. A clear stratum is observed in the upper third of the tube in which are occasionally seen colourless corpuscles and a few coloured. The colourless roll and the coloured also roll when they accidentally touch the tube on their edge. If not on edge, they merely turn over occasionally, exactly as a disc does in the large tube. The lower two-thirds of the tube are filled with coloured corpuscles. They crowd towards the lower part of the tube, but a considerable number of them being carried along with great rapidity in the axial stream, have a gliding motion. When the circulation of this blood is stopped and the tube filled with it observed for a few minutes, the whole of the blood corpuscles settle down to the bottom of the tube, leaving the serum above perfectly free.

EXPERIMENT No. 13.—*Defibrinated blood whose specific gravity has been raised to between* 1065 *to* 1070 *by the addition of common salt and egg albumin.*

Nearly the whole of the coloured blood corpuscles run in the axial stream. The clear area on the upper surface of the tube is not well marked, and the coloured corpuscles do not tend to accumulate on the bottom of the tube. The colourless are seen to move in the narrow clear area on the upper surface of the tube as before, and the separation of the two kinds of corpuscle is evident. There is not the same tendency for the coloured corpuscles when at rest to settle at the bottom of the tube.

EXPERIMENT No. 14.—*Defibrinated blood whose specific gravity is raised still higher by the same means.*

The coloured corpuscles are entirely displaced from the lower level of the tube. There is no well-defined clear area at the upper part of the tube and the axial stream is very well marked, a great many of the corpuscles being drawn into it. *They do not settle at the bottom* when *at rest.*

These experiments show that *by altering the specific gravity of the blood plasma through a range of something like* 1040 *to* 1080 *the coloured blood corpuscles can be made to float at any level. The lower the specific gravity the more they tend to come in contact with the bottom of the tube, the higher the specific gravity the more they rise to the higher levels. The nearer the natural specific gravity of the normal plasma is approached the more they occupy the axis and the quicker they move.*

EXPERIMENT No. 15.—*Circulation of Milk.*

Milk when passed through a horizontal capillary tube shows the following appearances:—The greater number of the particles float on the upper surface of the tube in the peripheral stream, but many of them run in the axis. The bottom of the tube is left perfectly clear. Those particles at the periphery rotate like colourless blood-corpuscles and have a great tendency to be arrested in their progress. Those in the

axis have a gliding motion. This was previously shown by Schklarewsky to be the appearance of circulating milk. He accounts for the separation of the particles into peripheral and axial strata by the difference in size of the particles. He says (*loc. cit.*) "the larger particles play the part of red, the small the part of colourless corpuscles." This is certainly not correct, there being in reality usually more of the large particles at the periphery of the stream than at the centre. The separation into these two layers is exactly what might be expected from the difference in the specific gravity of the globules of milk. If milk is allowed to stand even for a short time, we know that the particles which are richest in oil rise to the surface in the form of cream. There are many other globules, however, which do not rise to the surface even if the milk be allowed to stand for a lengthened period. They even do not sink to the bottom of the vessel, but remain suspended in the milk serum. The former are much lighter than the milk serum, the latter are apparently of exactly the same specific gravity. If these two kinds of milk globule are allowed to circulate through a tube, what we should expect from the experiments formerly recorded would, of course, be that the light particles would occupy the boundary, while those which are of equal specific gravity with the serum would float in the axis. This is what actually takes place.

There is another reason, however, why a large number seem to run in the axis, namely, that the globules are so numerous in the peripheral layer that they push each other more and more towards the axis, those which are driven inwards in this way being whirled along in the swift axial strata for a certain distance, and hence making it appear as if there were a greater inclination towards the axis than there really is. If milk be diluted with serum of the same specific gravity as that of the milk, so that there is present in the mixture only a small number of milk globules, then it is only occasionally that one of the peripheral globules gets into the axis, by far the greater number float on the upper surface of the tube.

EXPERIMENT No. 16.—*Defibrinated blood and milk mixed in various proportions.*

In all cases the blood corpuscles occupy the lower and the axial strata, the milk globules the upper and the axial. The milk globules behave in all respects exactly like leucocytes, rolling along, becoming arrested, and when the stream is slackened, accumulating in the upper part of the tube. When brought to rest the milk rapidly accumulates in the upper, the blood corpuscles more slowly in the lower part of the tube. The quicker the stream the less the milk globules tend to lag behind and to accumulate in its channel.

EXPERIMENT No. 17.—*Cinnabar particles.*

In experimenting with substances of this kind it is essential, of course, in order to avoid error, to see that they are perfectly pure. Pure cinnabar when circulated with water runs exclusively on the bottom of the tube. When mixed with half the quantity of milk the cinnabar still moves in the bottom of the tube, the milk in the upper levels. Both milk and cinnabar, therefore, circulate slowly and with some difficulty. The longer the tube, the more they tend to be arrested in it. The quicker the stream, the more rapidly they move; and if the stream be made very slow, the particles will not circulate, even although there may be a current in the centre.

Conclusions.—These experiments with a capillary tube exactly bear out, as will be noticed, what the previous experiments with the larger tube demonstrated, namely, that the situation occupied by bodies circulating in a tube depends upon *the relationship between the*

specific gravity of the bodies to the liquid in which they are suspended. Further, that the ease with which any suspended bodies will circulate depends, their size being appropriate to that of the tube, upon this relationship. The more they diverge in specific gravity from that of the suspending liquid the more friction is caused, and the more tendency there is to their becoming retarded and finally arrested in their progress.

Thoma's experiments (No. 13, lxxiv. p. 360) seem to fully corroborate these views. They consisted in examining the mesentery of a small warm-blood animal, such as a dog, guinea-pig, or cat, while it was immersed in salt solution of different strengths. He finds that with a 3 per cent salt solution the peripheral zone entirely disappears, and the coloured corpuscles come to occupy the whole lumen. The circulation is at first increased in rapidity, but very soon becomes slow and is finally arrested. The results, in all probability, are owing to an alteration in the specific gravity of the plasma produced by an increased transudation of water.

From these and the foregoing experiments we further learn of what immense importance it must be *to retain the specific gravity of the blood plasma at a proper level.* We have seen that a very slight decrease from the normal is sufficient to allow the coloured blood corpuscles to accumulate and run along the bottom of the tube. Did the same thing happen during life, we can imagine what a very serious result would ensue. The friction caused by the passage of the blood through the small vessels would thus be enormously increased, and there would be a constant tendency to stagnation. The milk stream circulates with great difficulty because its globules accumulate in the upper part of the tube. In the same way, if the plasma sinks below the normal specific gravity, the blood corpuscles will circulate with great difficulty—the whole blood stream will be retarded.

Albuminuria.—It is a fact familiar to every physician that *in extensive albuminuria there is a great tendency to inflammations of different kinds,* such as pleurisy, pneumonia, pericarditis, etc. Small hæmorrhages are also common in different parts, such as the retina, the pericardium, or serous coat of the intestine. There is also a tendency to hypertrophy of the left ventricle of the heart, and there is more or less general dropsy. May not many of these pathological phenomena be due to a wrong specific gravity of the plasma owing to the draining off in excessive quantity by the kidneys either of the water or the albumin? In *Asiatic cholera,* where the drain of water from the intestine is excessive, and where the cavities after death are peculiarly dry, the rapid collapse may be due to the same cause. The friction between the wall of the vessels and the corpuscles is too great to allow the heart to drive on the blood stream.

The subject is one which has received little attention, the general opinion being that any sort of fine particles will circulate exactly as the blood corpuscles do. There could not be a greater mistake, for it is certain that unless the relationship between suspended bodies and suspending liquid were properly balanced, the circulation through the complex capillary network of different organs could never proceed in the beautifully regular manner in which we know it does. The passive congestions, dropsies, inflammations, and hæmorrhages accom-

panying diseases affecting the composition of the blood, must be explained on some general cause. The above, in all probability, will be found in most cases to account for them.

The Application of the above-described Experiments to the Explanation of the Phenomena seen in the Circulation of the Blood Corpuscles.

156. From the foregoing it is evident that if the coloured corpuscles are nearly or exactly equal to, and if the colourless are specifically lighter than, the blood plasma, what takes place in their circulation is exactly that which we should expect—the coloured run in the axial stream, the colourless in the peripheral.

It has been frequently urged that we have no proof that the colourless corpuscles are specifically lighter than the plasma, because, it is said, if blood is allowed to stand, the colourless corpuscles do not gather in a layer on the top. Far from this disproving that the colourless are not specifically lighter than the plasma, it is only what should be expected under the circumstances. If we consider that the colourless in relation to the coloured are in the proportion merely of 1 to 600 or 700, it is surely not a matter for wonder that they are held down by the preponderance of the latter and will thus not be able to rise to the surface. Were the blood composed of bodies *all* specifically lighter than the liquid in which they are suspended, or were there a preponderance of such bodies, then the light particles would very soon come to the surface, but if the light be merely in the proportion of 1 to 600 or 700 of the heavy, and if the latter are of the same or of slightly greater specific gravity than the plasma, they will not rise to the surface but will be held down by the preponderance of the heavy.

It can be shown experimentally how this may be brought about by mixing small pieces of wax and Brunswick-green, very slightly heavier than water, with small pieces of pure wax in the same proportion as the blood corpuscles. Let these be suspended in a long narrow vessel with a quantity of water proportionate to that of the plasma of the blood. If the vessel is shaken so as to mix the two kinds of body together, and then brought to rest in the upright position, the pieces of pure wax do not necessarily come to the surface, but are held down by the specifically heavier and much more abundant pieces of wax loaded with Brunswick-green. How much more will this be borne out in blood placed in a vessel where there are millions upon millions of blood corpuscles heaped together, nay, tending to run together so as to entangle the leucocytes, and thus preventing the lighter specific gravity of the latter from asserting itself. Were the colourless corpuscles in greater number, it might only be expected that they would rise to the surface in a distinct layer in living blood.

It may, therefore, be granted that the only method by which the phenomenon of the separation of the blood corpuscles in the circulating current can be brought about, is by the colourless being specifically lighter, and the coloured of the same specific gravity as the blood plasma.

If this, however, be true, it might be said that all the colourless corpuscles should accumulate on the upper surface while the coloured should be all in the centre of the stream. Were the blood-vessels straight horizontal tubes, this would undoubtedly be the case, but

seeing that they twist in all directions and run at different levels, giving off branches and so forth, there will be a constant tendency to mixing of the two kinds of corpuscle, while it will be only at intervals that a separation of the white will occur. Those colourless corpuscles which are mixed with the coloured at the centre of the stream will not readily escape to the periphery. They will be carried along in the midst of the stream of coloured corpuscles running in the axis of the tube. It will only be when the colourless come near the surface of the mass of coloured corpuscles, or when the vessel and consequently the axial stream are very small, that they will tend to escape into the peripheral still layers.

It might be said again, however, that the colourless corpuscles, when they once escape from the axial stream, should all be found at the highest limit of the vessel. This also is not so necessary as at first sight appears, for, as seems very likely, when the leucocyte has escaped into the still layer and come in contact with the wall of the tube, it will tend to adhere by its friction to any portion which it touches. Any part of the upper half of the circumference of the vessel might therefore lodge a colourless corpuscle, its position depending greatly upon the part of the axial stream from which it has escaped.

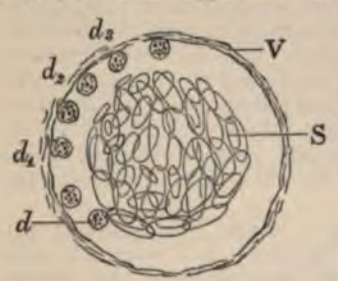

FIG. 72.

Thus in Fig. 72 let us suppose V to represent a vessel on transverse section and S the axial stream, it is evident that if a leucocyte escape from the axial stream at the point d it might easily find its way to either of the situations d_1, d_2, d_3, and by its plasticity become applied to the wall. This would be especially the case were the layers of liquid in the still area moving very slowly as in the veins. Hence we may encounter a colourless corpuscle in any of the situations represented by d_1, d_2, d_3, etc.

The colourless corpuscles accumulate more in the peripheral stream when the current is feeble than when it is brisk.

This, in relation to the diapedesis of leucocytes, is probably one of the most important facts connected with their circulation. It is well known that as stagnation is approached in an inflamed part the leucocytes tend to accumulate in the peripheral stream, while the coloured corpuscles still pass on in an even line in the axis. The explanation which is generally given (Thoma, Eberth, and Schimmelbusch) of the cause of this seems to be correct, namely, that it is owing to the slowness of the current, which, although insufficient to drive the specifically light colourless corpuscles onwards, is still competent to cause the coloured corpuscles, presenting as they do less resistance, to continue to circulate.

Eberth and Schimmelbusch (No. 13, vol. ciii. 1886) state that in the vessels of a warm-blooded animal four kinds of stream are noticed in accordance with its velocity—(1) The normal stream in which the axial current and peripheral zone are readily recognisable; (2) a slow stream in which the leucocytes accumulate in the periphery; (3) a still slower stream in which the blood plates also leave the axis and accumulate in the periphery, and in which, these observers assert, the leucocytes become less in number, although this would require confirmation; and (4) a stream so slow as to approach stagnation, in which all the elements of the blood are indiscriminately mixed.

The following experiment goes to support the above view:—

Experiment No. 18.—Arrange the large tube as before and let the stream at first be very slow. Introduce a small sphere of spermaceti and a disc made of wax and vermilion of the same size, but equal to the specific gravity of the water. It will be found that, while the disc readily passes through the tube, even with a very slow current, the sphere refuses to move or does so intermittently. The same can be demonstrated with two small spheres. If the rapidity of the current is now increased, everything is at once swept out of the tube. This demonstrates why the colourless corpuscles are found more abundantly in the peripheral stratum of the small veins where the current is slow, than in that of the arteries where the flow of blood is much more rapid. It also has an important bearing upon the accumulation of leucocytes in the periphery during inflammation, a subject presently to be referred to.

GENERAL CONCLUSIONS FROM ALL THE FOREGOING FACTS.

157. (1) The difference in position of the coloured and colourless corpuscles circulating in a vessel is not owing simply to the one being heavier than the other, but to the specific gravity of the coloured being nearly alike with the plasma, while that of the colourless is considerably less.

(2) The rotating motion of the colourless is due to their coming in contact with the wall of the vessel.

(3) The difference in their rapidity of motion is accounted for by their respective situations in the axial and peripheral streams.

(4) A certain rapidity in the flow of blood through the vessels is absolutely necessary to keep the colourless corpuscles circulating. Whenever this is diminished they tend to accumulate in the peripheral zone, and to obstruct the onward passage of the coloured.

CHAPTER XIV

INFLAMMATION—(*Continued*)

METHODS OF EXAMINING THE VASCULAR PHENOMENA

I.—Cold-blooded Animals.

158. **The Frog's Web.**—*Rana temporaria* (common English frog) is to be preferred to *R. esculenta*, as the web is more delicate. Nothing more is necessary than a piece of tin or other soft metal about $1\frac{1}{2}$ to 2 in. broad and about 6 to 8 in. long; or what is even better, a thin piece of hard wood of the same dimensions. At the end where the web is to be stretched, it should not be so broad. From the narrow end of this a V-shaped piece is cut out, over which the web is to be expanded. The frog should first be curarised, as this does not interfere with the circulation, provided that the solution employed be not too strong. The $\frac{1}{2000}$ of a grain, in watery solution, injected under the skin is sufficient. Chloral may be substituted. Caton (No. 9, x. p. 236) recommends a solution of 4 grs. to the drachm. As many minims should be injected subcutaneously as the frog is drachms in weight. The injection is made under the skin of the back with a morphia syringe. The animal is laid on the piece of metal or wood, and the web being stretched over the cleft at the end, the toes are held by tying a piece of thin thread to them and fixing the ends into a fine slit cut in the metal or wood. What will actually happen depends a good deal on the irritant used.

Thus Saviotti (No. 13, l. p. 592) divides irritants into two classes according to their effect. To the *first class* belong the greater number. When one of them is applied, *widening of the arteries, capillaries, and veins*, with simultaneous acceleration of the current, followed by contraction of the arteries, and slowing of the circulation take place. With this contraction may be associated (*a*) anæmia of the capillaries; (*b*) formation of a peripheral zone in the small and large veins, seldom in the arteries; and (*c*) stasis in the capillaries and small veins, seldom in the large, and never in the arteries. The *second class* comprises chiefly ammonia and its salts. They are distinguished from the former by the fact that they have scarcely been a]

plied before they are followed by a *contraction of the arteries* which he calls "primary," with a slowing of the current, appearances which last from a few seconds to one or two minutes. The subsequent changes are as in the first class. The vessels become widened, and in course of time again undergo contraction. He calls this contraction "secondary."

159. **Frog's Mesentery.**—The animal, which should be a male, is lightly curarised as before. To a plate of ordinary window glass a hollow cork about half an inch broad is cemented with Canada balsam or sealing wax. The frog is laid on its back on the plate, and a linear incision is made in the right side of the abdomen parallel with the middle line. If bleeding occur, the effused blood must be removed with some convenient absorbent material. A loop of intestine is now drawn out with a pair of photographer's horn forceps and stretched over the cork where it may be retained by introducing a few small pins through the intestine. As few of these, however, should be used as possible, as they tend to interfere with the circulation.

Klein (No. 16, p. 108) describes a very convenient little apparatus in which the mesentery is simply laid over a glass projection provided with a trough or groove at the margin in which the intestine is contained, without the use of pins.

It is essential to keep the mesentery moist, and this is best accomplished by removing the whole apparatus to a damp chamber while it is not under observation. As a rule, it is unnecessary to irritate it—the exposure to the atmosphere being sufficient to induce the inflammation. If, however, a more powerful stimulus be desired, so as to bring on the inflammatory phenomena more rapidly, a small plug of cotton soaked in cantharides may be introduced into the abdomen previous to withdrawing the intestine.

160. **The Frog's Tongue.**—The animal should again be curarised and placed on a glass plate with a cork fixed on to it as before. The aperture, however, should be more or less horse-shoe shaped (Klein) instead of circular, the convexity of the horse-shoe being towards the edge of the plate. The tongue is drawn out by two threads attached to the cornua, which, when the organ is fully extended, can be secured to pins. Care must be taken not to drag on the threads too much, otherwise the circulation may cease. Either the upper or lower surface may be examined, the position of the animal being altered accordingly. The surface should be moistened with serum from time to time, as it is liable to get dry. An artificial serum can be made with water 100, common salt 1, and albumin 10 parts (Caton).

When the circulation is thoroughly established, the tongue should be touched with some irritant (nitrate of silver) at one particular spot, and the phenomena noticed from hour to hour.

161. **The Frog's Lung.**—A frog having been narcotised, is laid on its back and an incision is made from the axilla downwards for about 1 inch. Care must be taken not to injure the lung in doing so.

When the tissues immediately overlying the lung are reached and punctured, a hernial protrusion of the lung follows. The opening is now enlarged with a probe pointed knife, and the whole lung springs out through the thoracic wall (Caton). This is not so convenient for studying inflammation as other transparent membranes.

162. **The Frog's Bladder.**—Prudden (No. 59, January 31, 1885), recommends this as specially convenient for studying diapedesis. The viscus is exposed by a lateral incision above the inguinal fold. The bladder is filled *per anum* with ¾ per cent salt solution by means of a bent glass cannula. The exodus of the cor-

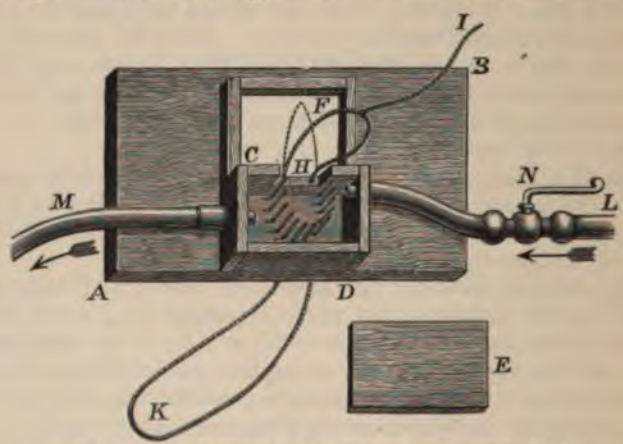

FIG. 73.—CATON'S APPARATUS FOR STUDYING THE TADPOLE'S TAIL.

puscles can thus be studied from hour to hour. The surface can of course be readily acted upon by irritants.

163. **The Tadpole's Tail.**—A tadpole should be selected which is losing its colour. From the fact that all the tissues are so beautifully seen as well as the circulation of the blood going on in the vessels, it has long been a favourite situation for studying inflammatory and reparative processes.

Tadpole Trough.—Caton (*loc. cit.*) describes an excellent tadpole trough for aiding in the examination of the tail.[1] "On a rectangular piece of gutta-percha AB (Fig. 73), 2 inches by 3, is built up a small trough CD (cover E is removed in the drawing to show the interior). A piece of glass CF, coinciding with an aperture in the gutta-percha, lies alongside the trough, and that side of the trough is cut down in its central part to the level of the glass, as shown at H. Adjacent to the opening thus made a semicircular cage of pin wire is seen inside the trough. A loop of silk thread IK passes through the plate by two small holes seen to right and left of H. A stream of water being caused to enter by the rubber tube L, and its amount regulated by the cock N, the trough is placed on the stage of the microscope and

[1] Dr. Caton has kindly furnished the author with the following two illustrations of his apparatus somewhat modified from the original, and also with the accompanying descriptions.

the instrument tilted at an angle of about 45°. The trough will keep almost full of water, and none will escape, excepting by the pipe M. A healthy tadpole is deposited from a teaspoon upon the plate CF. Its head at once passes through the opening H and under the loop of thread into the wire cage in the trough. The silk thread is gently drawn down at K. The tail will rest on the glass plate in the position shown by the dotted line. A cover-glass is laid upon it, and it is now ready for observation. It is desirable to use only a small stream of water."

164. **The Fish Tail.**—The circulation in the fish tail, on account of the delicacy of the tissues, is perhaps capable of more minute examination than that of any other part. Caton's apparatus (see Fig. 74) is the best adapted for the purpose of studying it.

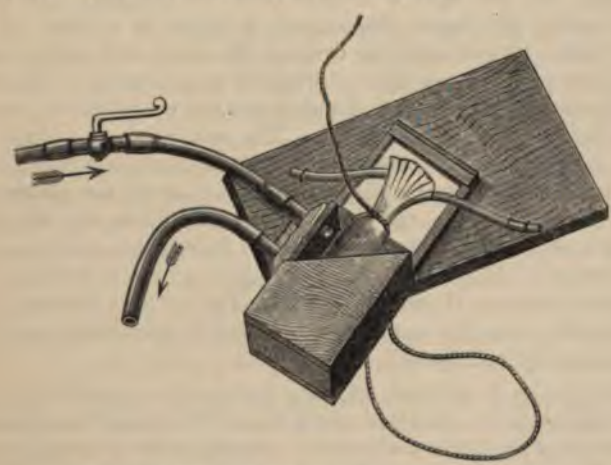

FIG. 74.—CATON'S APPARATUS FOR STUDYING THE FISH TAIL.

"It is similar in principle and in construction to the foregoing, excepting that the trough is larger and is placed obliquely, as shown in the woodcut. A loop of thread holds down the tail as before, but in addition, two small pieces of fine watch spring resting on the highest and lowest phalanges of the tail fin, hold it in the extended position. A small piece of cover-glass, triangular in shape, or a thin film of talc is laid on the tail."

II.—*Warm-blooded Animals.*

165. **Mesentery and Omentum.**—In order to examine these membranes in a warm-blooded animal, means must be adopted for keeping the membrane moist and at a constant temperature. From the fact of the omentum being so delicate in the guinea-pig, as well as from its anatomical relationship to the stomach, it is generally to be preferred to that of other animals. The omentum of the dog is also a very beautiful object. For the examination of the omentum of the former animal, Stricker and Sanderson (No. 9, x. p. 362) recommended some years ago an apparatus by which the temperature could

be kept pretty constant by an ingenious mechanical arrangement. Since then, however, the adoption of the mercurial thermostat (Sect. 77) has proved more convenient.

Thoma (No. 13, lxxiv. p. 360) describes a more complicated arrangement, which, however, has the advantage of being perfectly automatic as regards the renewal of the indifferent salt solution and the constancy of the temperature.

Eberth and Schimmelbusch (No. 13, ciii. p. 57) adopt a much simpler and more effectual plan than either of these. They employ a large vat with a glass bottom filled with salt solution, into which the entire animal is introduced. This is fitted on to the stage of the microscope, and the light is derived from the left side. In order to prevent soiling the liquid, the animal is wrapt in a sheet of gutta-percha tissue long enough to overlap the head, and made so as to enclose a funnel-like space through which it may breathe. The incision in the side for the purpose of drawing out the omentum or mesentery is made through the gutta percha. The salt solution is kept at an equable temperature by a thermostat, and is constantly renewed. As Thoma previously recommended, the object-glass of the microscope is sunk in the salt solution, the membrane meanwhile having simply been laid over a slide without any fastenings. Hartnack's dry lenses (Nos. iv., v., and vii.) do perfectly well and give excellent results. For a high power they use Hartnack's No. x. The vat just referred to is so made as to fit on to the stand of an ordinary microscope, so that the light can readily be adjusted.

Cheap vats, such as the above described, can readily be made of thin metal of different dimensions for animals of various sizes. They should be wide in front where the animal lies, but of the breadth of the stage of the microscope where the membrane is to be stretched out. Two tubes, one to convey the salt solution into the vat and another to conduct it away, are attached at opposite sides. These with a very little ingenuity can be connected with a vessel whose temperature is kept constant by means of a thermostat and Bunsen burner.

They recommend a mixture of chloral and morphia for narcotising the animal. Curari should not be employed for warm-blooded animals, as it reacts upon the circulation. For a full-sized guinea-pig, three grains of chloral injected subcutaneously are generally sufficient if chloral alone is used. If combined with morphia the dose should be less. The object is to keep the animal thoroughly narcotised, and it should be regulated accordingly.

Influence of the Nervous System.

166. Seeing that the vaso-constrictor and vaso-dilator nerves exert such an important influence in health on the regulation of the amount of nourishment supplied to the tissues, it comes to be an important question, in how far the vascular phenomena of inflammation are subservient to them.

The frog's hind limb has been the chosen seat of experiment in most observations on this subject. Here the question, however, arises, as to whether the sciatic nerve contains all the branches going to the web, or whether there are any other channels by which a stimulation of the cord, for example, may influence the vessels when the sciatic is divided.

Sanderson (No. 52, v.) holds the view that there are. He says that "the vascular nerves which supply the web *find their way by various channels to the arteries* to which they are distributed, so that there is no single trunk by the division of which these vessels are completely paralysed." He supposes that the distribution may even vary in different individuals.

Lister, during his classical researches on the parts of the nervous system regulating the contractions of the arteries (No. 65, 1858, p. 607), found that an artery in the limb of a frog showed spontaneous contractions nine days after amputation, and he concluded that there exists within the frog's limb some means, probably ganglionic, by virtue of which the arteries may contract in concert with each other, independently of any ganglia contained in the trunk.

Certain stimuli applied directly to the web cause a contraction both of the arteries and veins of the web. Thus Paget (No. 23, Chap. xiii.) showed that if a fine needle be drawn across the web three or four times, without apparently injuring the membrane, they will both gradually contract and close. After holding themselves in the contracted state for a few minutes; they will begin again to open, and slowly dilating, will acquire a larger size than they had before the stimulus was applied. When dilated they will not again readily contract to the same stimulus, but if a stronger stimulus be employed contraction will follow. Such a secondary contraction, if brought about by a cautery, may last more than a day.

Saviotti in his well-known paper (No. 13, l. p. 592) states that when the skin of the frog is peripherally stimulated, as by tapping it on the abdomen or by pinching it with a needle, the arteries of the web contract. The contraction ceases after a few seconds, and returns on the stimulus being reapplied. As a rule, he saw no contraction take place in the veins. A slight stricture was occasionally noticed within them, but he questions whether this was the same as the well-marked contraction seen in the arteries.

It is well known that slow rhythmical contraction, not synchronous with the heart's beat, occurs in the arteries of transparent parts such as the ear of the rabbit, the bat's wing, and frog's web (Schiff, Golz, and Mantegazza). Wharton Jones, moreover, has described (No. 65, 1852) a rhythmical contraction as taking place in those veins of the bat's wing which have valves. Several questions of importance are raised by these facts—(1) whether the above contractions are of a truly rhythmical character; (2) whether they are reflex phenomena; or (3) whether they are dependent upon the heart having been inhibited through the pneumogastrics. Golz (No. 13, xxvi. p. 1) and Mantegazza (No. 57, v. 1866) long ago showed

that stimulation of a sensitive nerve causes weakening of the heart and diminution of the force of the pulse waves. It is now also well known, as Sanderson (No. 52, Article "Inflammation") points out, that some of the modes of irritation employed by Saviotti influence not merely the vaso-motor nerves, but also the vagus heart nerves. Thus the well-known experiment of arresting the movements of the heart in a state of diastole by tapping on the belly of a frog acts in the same way as direct stimulation of the vagus itself.

Saviotti, however, cuts the sciatic, and finds that no more contraction follows, and hence concludes that the contractions must be reflex in their nature. He affirms that a stimulant applied to any part of the body calls forth a reflex contraction of the arteries, and that this is independent of the contraction of the heart.

Division of Sciatic.—Considerable difference of opinion prevails in regard to the effect of this on the blood-vessels of the frog's web, as well as to what follows on subsequent stimulation of the divided ends.

Lister (*loc. cit.*, p. 609) found that, on tying a ligature round the sciatic nerve of a frog, distinct contraction of the arteries occurred within the first few seconds, which, within the next two minutes, had given way to a dilatation. In half an hour afterwards the artery under observation had again contracted to about its usual proportions, and a few minutes later the constriction of the artery was very considerable and continued after section of the nerve above the ligature. The arteries of the other foot were similarly contracted. It was evident that the arteries had experienced no permanent dilatation from the division of the sciatic nerve—a result, he says, quite at variance with the experience of previous observers.

Saviotti (*loc. cit.*) found that in the majority of cases the simple division of the nerve caused first a widening of the arteries, and afterwards of the other vessels. This dilatation, however, was more evident in weakly than in vigorous frogs. With the dilatation a simultaneous acceleration of the current followed. Stimulation of the divided end of the distal portion by pinching it, he states, causes so much contraction of the arteries of the web that a slowing and ultimately a cessation of the circulation within them follows. Sanderson (*loc. cit.*), however, does not find that this takes place with the constancy which Saviotti vouches for; and thinks that the distribution of the vascular filaments of nerves may differ in different individuals.

When the central end of the divided nerve, however, is stimulated, very definite results ensue, as Riegel (No. 46, 1871) has shown. A distinct acceleration of the current is one of the chief phenomena, and this, Riegel affirms, is associated with a slight contraction of the vessels. Although the acceleration of the stream in inflammation is associated with dilatation of the vessels, yet Sanderson holds to the view that there may be certain states of the arteries in which an accelerated flow of blood may be associated with persistent reflex arterial contraction.

When the nerve is not divided, but is simply raised from its sheath, Saviotti (*loc. cit.*, p. 611) asserts that irritation of it by pinching causes a sudden cessation of the circulation in the web, which passes off as the pressure is removed. He could sometimes cause this phenomenon to recur a second and third time in the same animal.

The question, however, for us at present to consider is in how far such nervous influence is necessary to induce the inflammatory phenomena. Cohnheim (No. 31, i. p. 228), after passing in review Saviotti's experiments, expressly emphasises the opinion that "these phenomena have nothing to do with inflammation." He refers to the

fact that inflammations are specially prone to occur in parts deprived of their nerve supply, such as the *cornea after division of the fifth nerve*, and in cases of *ordinary paraplegia*. The occurrence of *herpes zoster* along the course of the intercostal nerves is often quoted as an instance of an inflammation induced by and localised to the area of distribution of a definite set of nerves. As Cohnheim, however, remarks, it would require further experimental proof to demonstrate that the nerve trunks are so actively concerned in the production of this peculiar disease.

The two experiments that are usually quoted as bearing upon the question are those of *division of the fifth nerve* and that of the *pneumogastric* or *recurrent laryngeal*.

When the fifth nerve is divided in a rabbit, the eyeball becomes very liable to inflammatory destruction (Magendie, 1824). Snellen (No. 80) accounts for this by the loss of sensibility allowing foreign matters to impinge upon the cornea without inconvenience to the animal and thus irritating it. Friedländer (No. 13, lxviii. p. 325) showed that division of the recurrent laryngeals or pneumogastrics in a rabbit induces in a short time a form of pneumonia. The explanation of this, however, seems to be that the paralysis of the larynx resulting from the operation allows particles of food to be inspired, and that it is these which excite the inflammation. *Division of the sympathetic in the neck* brings about increased vascularity, but not inflammation.

It seems more likely that most of the vascular phenomena in inflammation are owing more to purely physical causes connected with the circulation of the solid bodies suspended in the blood than to actual nerve action. One of the chief influences which the vaso-motor nerves evidently exert upon the vessels in health is in preventing the undue fluxes which otherwise are constantly liable to take place in parts where nerve control has been lost.

Whatever may be the influence of the nerves upon the production of inflammation, Jankowski's experiments (No. 13, xciii. p. 259) seem to prove that the division of the sciatic in the dog has the effect, probably by paralysing the vaso-motor nerves and increasing the distensibility of the vessel walls, of causing an increased flow of lymph from an artificially inflamed part. He inflamed the paws of two extremities in the dog, and after the inflammation had lasted for some time, he divided the sciatic nerve in one limb. On placing cannulæ in the main lymph vessels returning from the limbs, he found that the quantity was much greater on the side on which the nerve had been divided than on the other, and also that the œdema of the parts was greater on this side than on the opposite.

Literature on Influence of Nervous System in Inflammation.—**Ayres** (Sympathetic): Arch. f. Ophthal., xi. 1882, p. 199. **Disselhorst**: Fortschr. d. Med., v. 1887, p. 289. **Dujardin** (Trophic Keratitis): Rev. Clin. d'Ocul., v. 1885, p. 191. **Hallopeau and Neumann**: Compt. rend. Soc. d. Biol., v. 1880, p. 309. **Jones (C. H.)**: Med. Press and Circ., iii. 1867, p. 159. **Lizars**: Edin. Med. and Surg. Journ., xv. 1819, p. 396. **Shaffer** (General Irritation): Ann. Anat. and Surg., Brooklyn, iv. 1881, p. 45. **Snellen**: Arch. f. d. holländ. Beitr. z. Nat. u. Heilk., i. 1858, p. 206. **Travers**: Constitutional Irritation, etc. 1835. **Weber**: Centralbl. f. d. med. Wissensch., ii. 1864, p. 145. **Wood**: Edin. Med. Journ., 1856, ii. p. 586.

Vascular Phenomena of Inflammation.

A. *Cold-blooded Animals.*

167. **Mesentery of Frog.**—When withdrawn for examination, the first thing noticed is a **widening of the vessels.**[1] The application of a severe stimulant to a part usually induces momentary contraction of the vessels (Lister). It has been asserted that such momentary contraction follows the simple withdrawal of the loop of intestine from the abdomen, but by the time that the mesentery has been adjusted for observation this has vanished. The dilatation takes place primarily in the arteries, afterwards in the veins and capillaries, and it usually requires from fifteen to twenty minutes up to two hours before it is complete. So great can it become that the vessels may in time present twice their normal calibre.

With the dilatation of the vessels **an increased rapidity in the circulation of the blood through them follows,**[2] most evident in the arteries, but also present in the veins and capillaries. Sooner or later, however, **the accelerated blood stream begins to diminish,** again becomes normal, and finally, **slower than usual.** In the exposed tongue of the frog, irritated by application of nitrate of silver, there is often no stage of acceleration, but the vessels immediately dilate and the current rapidly diminishes within them.

On account of this dilatation, the number of capillaries is apparently increased. As W. Jones originally pointed out, many of them have become evident which previously were invisible, and consequently the part has a redder colour.

The corpuscles of both kinds next begin to accumulate in the capillaries in great number, and **a greater separation of the colourless from the coloured takes place in the small veins.** The former also have a greater inclination to lag behind. More colourless corpuscles are consequently seen in the peripheral part of the stream than before, and these often become arranged in little heaps or masses. This peripheral zone of leucocytes is noticed both in the veins and smallest arteries, but primarily, and to a far greater extent, in the veins.

As previously demonstrated, the increased tendency to separation of the leucocytes from the coloured blood corpuscles is to be accounted for by the gradual slowing of the stream (see Sect. 156, experiment No. 18). A far more beautiful experiment can, however, be made for the purpose of demonstrating this by means of the apparatus delineated in Fig. 75.

[1] Why the vessels should thus spontaneously dilate has never been satisfactorily explained. The author believes that it may be caused by the removal of the counter-pressure afforded by the walls and contents of the abdomen. Consult Duncan on "Retentive Power of the Abdomen" (No. 197, Part v., p. 409); and John Bell (No. 198, p. 327.) See also Sect. 194 *et seq.*, in relation to this subject.

[2] This is usually supposed to be dependent upon the dilatation. Schiff (No. 71) and Sanderson (No. 52) affirm that dilatation has exactly the opposite effect.

It consists of a series of continuous curved glass tubes (*a*,*a*,*a*), supported on uprights as before, through which water may be circulated. As there is considerable difficulty in driving the air out of the tubes, the upper curves are provided with stop-cocks (*b*,*b*,*b*,*b*), by which the air contained in the tube can be released. Each bend in the tube is attached to its neighbour by a metal coupling (*c*,*c*,*c*), which renders the danger of fracture less. To the supply pipe at the entrance to the series of curves, a long tube (*d*) is welded or united by a metal coupling for the purpose of introducing the bodies to be circulated. The end of the exit tube (*e*) is placed in a vessel filled with water to prevent any regurgitation of air that might happen when the circulation is stopped. The whole apparatus stands in a metal trough provided with an escape pipe (*f*), and into this trough the overflow runs.

A number of very instructive experiments can be made with this apparatus. One which is specially related to the separation of the leucocytes, and their tendency to lag behind as the current diminishes in rapidity, is the following:—Let the stream circulating through the system of curved tubes be very weak. Introduce

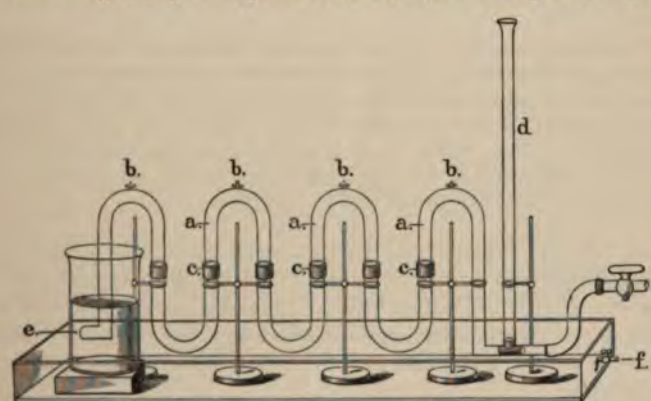

FIG. 75.—APPARATUS FOR ILLUSTRATING THE ACCUMULATION OF LEUCOCYTES IN THE VESSELS WITH A SLOW CURRENT.

through the upright tube a small sphere of spermaceti and a disc of wax and vermilion, so made as to be of the same specific gravity as the water. Both, of course,[1] readily pass up the ascending limb of the first curve, but whenever the bend of the tube is reached it will be found that while the disc glides with the greatest facility round it, the sphere catches in the bend and refuses to circulate. This occurs quite irrespective of their shape, and is due, as before explained, to the difference in their specific gravity (Sect. 151).

If the stream be now increased in velocity it will be found that the sphere is swept along, certainly not with so great facility as the disc, but still with such ease that it readily circumvents all the curves in the tube.

This experiment is a complete verification of what occurs in inflamed parts. It is at the bends in the blood-vessels that the leucocytes chiefly catch. In the arteries, of course, there is less tendency to separation than in the veins, because the stream is more powerful.

The veins now assume an appearance as if the internal surface of their wall were plastered over with leucocytes (Cohnheim), and in the

[1] Two spheres of small and equal size answer the purpose as well.

capillaries a similar adhesion of the leucocytes to the wall is noticed. They, however, alternate, and are abundantly mixed with the coloured in the latter situation.

As this peripheral sheath of colourless corpuscles forms, further changes may be observed in it. **Those corpuscles which are nearest the wall become flatly applied to it, and soon outside the wall there are noticed little rounded buds or projections consisting of pseudopodial processes of the leucocytes within.** Each little bud-like body increases in size, while the mass of the corpuscle within the vessel diminishes, and ultimately **the whole of the corpuscle manages to escape through the vessel wall** (see Fig. 77). Numbers of other corpuscles make their exodus in the same manner, so that, in course of time, a dense mass of escaped leucocytes accumulates round the vessel.

So improbable does this escape of leucocytes through the wall of the vessel appear to many minds, that even so acute an observer as Mr. Wharton Jones, whose work on the vital phenomena of Inflammation (No. 63, vii. 1851) will always remain a monument of accurate observation, so lately as the year 1884 (No. 59, October 11), denied that he had ever been persuaded of its actual occurrence; and explained the appearance of the vessel coated outside with leucocytes by tracing it to proliferation of the endothelial nuclei of the wall.

This process of diapedesis is, to a certain extent, a natural one, seeing that it occurs normally in the tail of the tadpole and elsewhere (Caton, No. 5, 1871) during health. Stricker, moreover, has shown that the *coloured* corpuscles exude in the same way in frogs under the influence of curari. The inflamed condition is merely an exaggeration of the natural.

The diapedesis is noticed in the veins after the peripheral zone of leucocytes has formed, but in the capillaries it goes on all along from shortly after the time of exposure. It commences in the veins as the current begins to slacken pace; is most abundant when it becomes very slow; and ceases with complete stagnation (Cohnheim). It is not evident in the arteries until the inflammation has lasted for many hours, and even then it is comparatively exceptional to see it.

In the course of twenty-four to thirty-six hours it will also be found that **the coloured corpuscles are extravasated in large number,** either from actual rents in the blood-vessels, or from their having escaped between the endothelial plates in the same manner as the leucocytes.

As the diapedesis is going on, the circulation, as stated, is becoming slower. **A to and fro oscillation of the current** is now noticed in some of the larger arteries, as if they were making a vigorous effort to drive the blood onwards. Finally, however, even this motion of the blood-column ceases, and **complete stasis or stagnation is attained.** The stasis is usually seen first in those capillaries which are in the least direct course from an artery to a vein—that is to say,

it occurs first in those vessels in which the *vis e tergo* is weakest (W. Jones).

The blood in the stagnated vessels, as Paget (No. 23, Chap. xiii.) observes, has little tendency to coagulate, hence the possibility of re-establishing the circulation when the acute symptoms have subsided.

By this time the lymph spaces round about the small veins and capillaries are loaded with blood corpuscles of both kinds, chiefly the colourless; and now a great many of these seem to make their way on to the *upper* surface of the mesentery, where along with fibrin precipitated from the exuded liquid they may constitute a **false membrane.**

168. **Tongue of the Frog.**—When the tongue of the frog is touched with nitrate of silver, the following, according to Cohnheim (No. 60), are the phenomena which progressively ensue in and around the eschar which it produces.

The almost momentary effect is to cause slight muscular twitchings of the tongue, followed by rapid dilatation, primarily in the arteries running to the cauterised spot, subsequently in the veins returning from it. An extreme hyperæmia of the capillary vessels in and near the irritated part is next noticed, which may extend for a considerable distance into neighbouring parts. With the dilatation, as in other inflamed tissues, the blood flows at first with great rapidity. Soon, however, matters change, in that the rapidity of the circulation within the vessels is seen to be falling off, and mainly in those vessels which ramify through the cauterised spot. The artery in vain endeavours to drive the blood onwards, and finally, complete stagnation within the cauterised area is attained. Both in the case of the arteries and in that of the veins, this stagnation prevails up to the first collateral branch met with outside the point of irritation. In the parts around, the circulation is still proceeding with unusual activity, although in some of the capillaries in the immediate neighbourhood stasis has also occurred.

All these phenomena are induced, of course, mechanically by the action of the caustic. *There now succeed others* which are of a different nature, and which may be denoted inflammatory. In an hour or two after the cauterisation these *dilated arteries* which are at the greatest distance from the point of application *show signs of contracting*, and this is followed by a *diminished rapidity in the flow of blood* in the veins in communication with them. Those arteries which are nearer the point of irritation shortly afterwards become similarly contracted, and the stream within their veins consequently diminished in velocity, until there arrives a time in which the rapidity of the flow of blood within the surrounding parts becomes normal. Sometimes in those large arteries and veins going directly to and from the eschar the dilatation remains permanently, but even in these, a gradual slowing of the current becomes perceptible.

While the larger vessels have thus been contracting, not less striking phenomena are noticeable in *the capillaries*. Those which are farthest away from the eschar have been gradually getting quit of their excessive blood under the influence of the contraction of the arteries, and now again present the yellow appearance of their natural state. In those, however, which are nearer the central point of the inflamed area the stasis remains as before; and the corpuscles within them undergo a peculiar transformation by which they appear to become fused into a homogeneous bluish-red colloid-like mass.[1]

[1] This appearance is generally supposed to be due to diffusion of the hæmoglobin of the corpuscles. Eberth and Schimmelbusch, however (No. 13, ciii. 1886), regard it as an effect of pressure.

Around this region of perfect stasis is one of broader or narrower dimensions, in which, although the stasis may not be complete, yet the circulation within the capillaries is certainly very slow; but beyond this, in other parts of the tongue, the circulation is perfectly normal. As regards the time at which these appearances occur, it varies so much in different animals that it is impossible to limit it at all strictly. As a rule, however, it may be said that this is the condition of parts in *from six to eight hours after the application of the irritant.*

During the *following six to eight hours,* changes of great import are to be noticed. In the immediate vicinity of the eschar which has now become black, some of the arteries and veins, especially the former, still present evidence of considerable dilatation; but the dilatation is limited to the neighbourhood of the eschar. Within the dilated parts the circulation is extremely sluggish. There now ensues a process of the greatest importance, namely, *extravasation of the blood corpuscles.* Along the inner surface of the wall of the small veins colourless corpuscles have been noticed to be accumulating as the circulation diminished in velocity; and these, almost to the exclusion of the coloured corpuscles, are found to pass through it, while in the case of the capillaries *both kinds of corpuscle are seen to escape.* This process of diapedesis from having been local at first now becomes general throughout the area of inflammation, but is not noticed within the zone of congested capillaries immediately around the eschar. These remain perfectly free from any evidence of corpuscular extravasation. Both veins and capillaries become ensheathed in a deep layer of them.

During the next two days the diapedesis goes on increasing, and occasionally a coloured corpuscle manages to escape from a small vein at this period, although *the leucocytes pass out in far greater numbers.*

In the vicinity of the eschar the blood corpuscles tend to accumulate, and as time goes on, it is evident that the coloured corpuscles are being increasingly extravasated. These, from their colour, are more evident than the colourless, but the latter can be seen lying among them in the infiltrated zone. Towards the periphery the coloured corpuscles become less numerous, so that the colourless outnumber them. *The lymph spaces of the tongue,* especially the lymph sinus situated posteriorly, also *contain many leucocytes,* and the lymph sacs are often tense from having absorbed excess of fluid transuded from the distended vessels around the eschar.

Things thus remain *in statu quo* for several days, but ultimately the excessive transudation of fluid and extravasation of blood corpuscles ceases, and *those colourless corpuscles which had accumulated round the eschar are removed.* The coloured corpuscles in this locality remain, however, considerably longer. It is usually a matter of *weeks before the eschar becomes detached.*

B. *Warm-Blooded Animals.*

169. The phenomena here do not differ materially from those observed in the frog, except as regards the presence and disposition of the hæmatoblasts or blood plates. In the mesentery of the dog or guinea-pig there are the same axial and peripheral currents as in a cold-blooded animal. According to Eberth and Schimmelbusch (No. 13, ciii. 1886), the blood plates in the normal stream run in the axis along with the coloured blood corpuscles, and hence they hold that they must be of very much the same specific gravity. A few of the colourless also flow in the axial current, but the largest number

are rolled along in the peripheral part of the lumen. The peripheral plasmatic zone, they state, runs from ten to twenty times slower than the axial stream. As the current becomes slower during inflammation,

FIG. 76.—PORTION OF OMENTUM OF YOUNG DOG EXPERIMENTALLY INFLAMED AND SUBSEQUENTLY STAINED WITH SILVER (×50 DIAMS.)

(*a*) Small vein surrounded by extravasated leucocytes; (*b*) larger vein in same condition; (*c*, *e*) the fenestræ of the membrane whose walls are covered by sprouting cells.

the leucocytes are picked out from the mass of circulating corpuscles, and tend to become arrested at the periphery; and as it gets still slower, the blood plates also leave the central stream and accumulate in the peripheral zone (see Fig. 65, C). Finally, the whole

of the corpuscles, as stasis is approached, become indiscriminately mixed.

The exudation of leucocytes, as may be most beautifully demonstrated by artificially inflaming the mesentery in a young dog, and subsequently staining it with silver (see Figs. 76 and 77), goes on exactly as in a cold-blooded animal; and in Man, where the case is

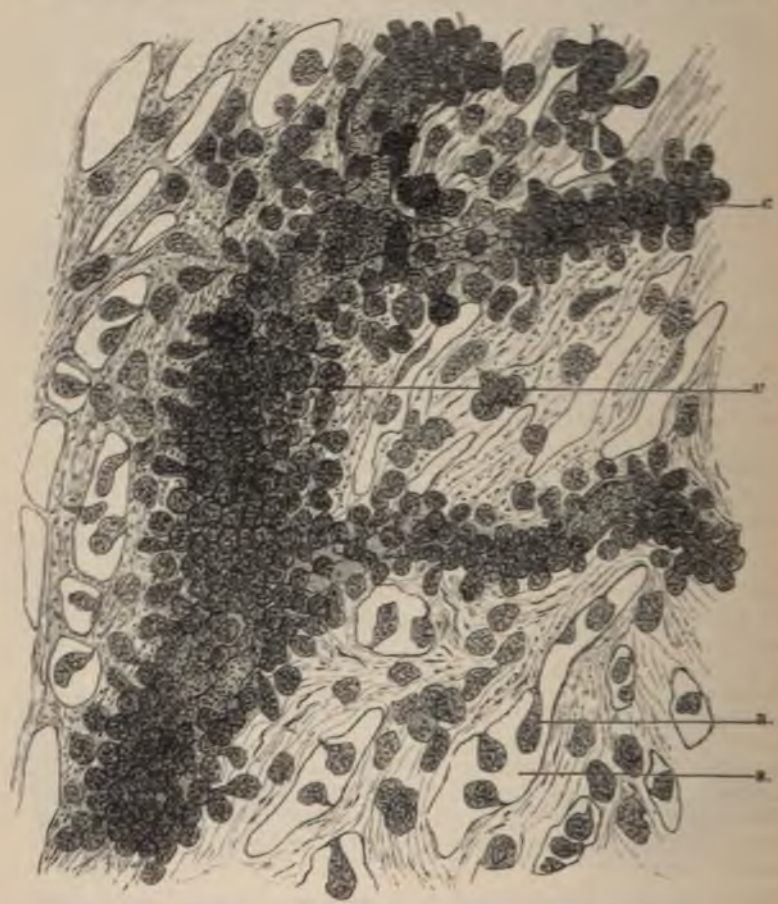

FIG. 77.—PORTION OF SAME OMENTUM AS IN FIG. 76 (×450 DIAMS.)

(*a*) Pyriform cell, probably of endothelial origin, sprouting from wall of a fenestra [*s*] of the membrane; (*c*) capillary surrounded by extravasated leucocytes; *v*, small vein in similar condition.

suitable, identical phenomena will be noticed when death has resulted from peritonitis.

We may therefore conclude that the phenomena just described are alike common to warm and to cold-blooded animals.

HISTORY OF THE DISCOVERY OF DIAPEDESIS.

170. It is generally supposed that Waller (No. 61, xxix. 1846, pp. 271, 298, 397), from his observations on the tongue of the frog, was the first to recognise this remarkable phenomenon. He not only described the passage of the corpuscles through the wall and gave accurate drawings, but in opposition to the blastema theory of formation of pus and other cells then in fashion, he clearly indicated that the pus corpuscles found in inflamed parts were identical with the colourless corpuscles of the blood. It had been previously surmised by certain observers that the corpuscles of the blood gave rise to those found in mucus and pus, and that they escaped by a process of extravasation or filtration. Waller, however, by his experiments upon the frog's tongue clearly demonstrated the fact, and held that he had discovered the porous character of the vessel wall so long supposed by physiologists to exist.

Horwath (No. 40, xcix. 1884, No. 26) has drawn attention to the fact that the phenomena of diapedesis must have been familiar to Dutrochet many years before Waller had so graphically described them. Dutrochet's observations are contained in his *Recherches Anatomiques et Physiologiques*, and the observations which he records were made in the year 1824 on the tail of the tadpole of the toad. He states that he saw certain corpuscles leave the vessels and move slowly into the surrounding transparent tissues, from whose granules they were no longer to be distinguished. He supposed that the cells of the tissues, were nothing more than these cells which had become fixed, and that they explained the *rôle* played by the blood in nutrition. He was not clear about the manner in which they escaped. Perhaps there were small openings in the wall of the vessel, or it might be small channels in communication with the vessel in which they were confined.

In his essay on *Inflammation* (No. 62), published in the year 1843, and subsequently in his work on *Consumption and Scrofula*, published in 1849, Addison clearly pointed out the relationship of the colourless corpuscles of the blood and the pus corpuscles lying round the vessels in inflamed parts. The following passages are taken from the latter work:—"During inflammation—using the word in the general sense here indicated—there is more or less marked increase of the colourless elements and protoplasma in the parts affected. At first—in the first stage—these elements adhere but slightly along the inner margin or boundary of the nutrient vessels, and are therefore still within the influence of the circulating current; belonging, as it were, at this period as much or rather more to the blood than to the fixed solid. Secondly—in the second stage—they are more firmly fixed in the walls of the vessels, and, therefore, now without the influence of the circulating current. Thirdly—in the third stage—new elements appear at the outer border of the vessels, where they add to the texture, form a new product, or are liberated as an excretion."[1]

Cohnheim (No. 13, xl.), unaware of the publications of Waller and Addison in the year 1867, again described all the phenomena in terms almost identical with the former. It was the appearance of this paper which in reality drew attention to the occurrence of diapedesis, and since its publication the facts recorded in regard to the escape of blood corpuscles through the vessel wall have been almost universally accepted.

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[1] Zimmermann (No. 67, 1852) is generally regarded as being the first in Germany to have stated that the exudation in inflammation is composed of colourless blood corpuscles. He supposed that they came from torn capillaries.

MANNER IN WHICH THE CORPUSCLES ESCAPE.

171. As just stated, the idea of the walls of the vessels being porous dates as far back as the time of Dutrochet. It was of late revived by Arnold (No. 13, lxii.), based upon the fact that when small veins and capillaries are injected with nitrate of silver, little black points are seen in their walls, which he supposed were small apertures or stigmata. When a coloured injection of gelatine is driven into such silver-stained vessels the injection mass seems to escape at these points. That they are actual apertures, however, in the wall has been denied by Cohnheim, Lassar, and others who have studied the subject, and of late Arnold himself has retracted the opinion that they are such. They seem to be simply portions of the cement between the endothelial cells.

Norris, in a communication made to the Royal Society, endeavoured to prove by a number of well-known facts in regard to the passage of solid bodies through soap-bells, that the wall of a capillary resembled physically a thin film of solution of soap, and that the corpuscles migrated through it without rupture. One can hardly believe that this is so, otherwise how would the capillaries be sufficiently strong to withstand the blood pressure within them, which is considerable? A more probable view is simply that the attachment of the endothelial plates becomes loosened in parts. This allows of a certain amount of separation, and the corpuscle gradually makes its way outwards through the resulting clefts. Cohnheim (No. 31, i. p. 236), in fact, looks upon inflammation as simply the expression and result of a molecular alteration of the vessel wall, allowing, as it does, an increased transudation of liquid and the passage of blood corpuscles.

The Colourless tend to emigrate more than the Coloured.—In the early stages of inflammation, more especially where it is induced gradually, the *colourless corpuscles* certainly exude in greater abundance than the *coloured*. The cause simply seems to be that they accumulate in the peripheral zone of the vessels as the current slackens, and that they are applied at first hand over the openings between the endothelial plates. It has been shown, however, in the description of the phenomena in vascular parts (Sect. 167 *et seq.*), that in the later stages of the process the coloured also emigrate in large numbers. When the inflammation comes on *suddenly*, as in certain forms of pneumonia, the coloured are extruded at first in as great, or in greater, numbers than the colourless. Cohnheim (No. 31) has shown, when the vein returning from a frog's limb is *suddenly* ligatured, that the coloured corpuscles exude in far greater abundance than the colourless. In these cases it is evidently the *suddenness* with which the venous obstruction is brought about that is the cause of their extrusion. Time has not been afforded for the peripheral layer of leucocytes to form, and hence the whole of the solid blood contents are extruded.

Literature on Diapedesis.—**Beale**: Med. T. and Gaz., 1868, i. p. 496. **Balogh**: Arch. f. path. Anat., xlv. 1869, p. 19. **Damman**: Ueb. d. Bedeutung d. farblosen Blutkörperchen f. d. Pathologie, 1868. **Duval-Jouve**: Montpel. Méd., xxviii. 1872, p. 333. **Geltowsky** (Action of Quinine on D.): Practitioner, viii. 1872, p. 321. **Heger**: Étude critique et expérimentalle sur l'Emigration des Globules du Sang, 1878. **Kerner** (Action of Quinine on D.): Arch. f. d. ges. Physiol., v. 1872, p. 27; *Ibid.*, vii. 1873, p. 122. **Leissler**: Ueb. d. Austritt d. Blutkörperchen a. d. Gefässen, 1868. **Norris**: Birm. Mid. Review, i. 1869, p. 542. **Purves**: Arch. néerl. d. Sc. exactes, etc., ix. 1874, p. 374. **Ramon-y-Cajal**: Rev. esp. de Oftal, Madrid, ii. 1881, p. 238. **Rotch**: Emigration of White Corpuscles, Camb., 1873. **Rouget**: Arch. de Physiol. norm. et path., i. 1875, p. 821. **Schklarewsky**: Arch. f. path. Anat., xlvi. 1869, p. 116. **Schmuziger**: Arch. f. mik. Anat., ix. 1873, p. 709. **Stricker**: Untersuch. üb. d. Lehren d. farblosen Blutkörperchen d. Menschen, 1867. **Tarchanoff**: De l'Influence du Curare sur la Quantité de la Lymph et l'Emigration, etc. **Thoma**: Die Ueberwanderung farbloser Blutkörper v. d. Blut in d. Lymph-gefässsystem, 1873.

CAUSE OF THE STAGNATION.

172. Several different views have been held from time to time regarding this, and, as yet, it is hard to say whether the matter has been thoroughly explained. It is questionable whether it be the same in all cases. That it seems to be independent of the general circulation is borne out by the experiment originally devised by H. Weber in 1852 (No. 64, p. 361), and repeated by Lister (No. 65, 1858), namely, that if a ligature is tied round the thigh of a frog so as to obstruct the circulation, and the web be irritated with ammonia, the blood corpuscles crowd into the capillaries of the irritated spot until they are distended and engorged with them.

Lister (*loc. cit.*), from experiments on this subject, arrived at the conclusion that the *wall of the inflamed vessel acts as a foreign body in causing the corpuscles to run together and to adhere.* In the natural vessel they have no tendency to do so. Other observations on this matter have been made by Ryneck (No. 66, 1870) and Cohnheim (No. 31), all of them more or less unsatisfactory.

A more probable explanation was given by Wharton Jones, namely, that the abstraction of the liquid part of the blood as it transudes from the distended vessels *leaves the blood corpuscles in a relatively too dry condition* to circulate. He has shown that when a strong solution of common salt is applied to the exposed web, stagnation occurs very rapidly, the explanation evidently being the abnormal osmotic conditions set up in the part. The corpuscles in the capillaries are left in a comparatively dry condition, and consequently they progress at first slowly and with difficulty, while ultimately their progress is completely arrested. The corpuscles also tend to adhere, and this no doubt aids in completing the stasis. It may be mentioned, however, that Lister (*loc. cit.*) strongly opposes this view, and brings certain striking arguments to bear against it.

When the mesentery is under observation stasis can be averted for a very long time by keeping it in a *moist atmosphere*, but the slightest drying of the membrane at once brings it about. Under other circum-

stances the stretching and attenuation of the capillary wall no doubt favour transudation of liquid, so that in time the friction between the wall and the blood-stream becomes so great that the column of corpuscles refuses to progress.

Thoma's experiments (No. 13, lxxiv. p. 360, 1878), previously referred to seem to bear this idea out. He finds that by immersing a coil of intestine and mesentery of a warm-blooded animal in different strengths of salt solution, the almost immediate effect is, in most cases, to hasten the speed of the circulating blood, followed very soon afterwards by slowing and stagnation.

It is possible, however, that another cause is at work which may aid in obstructing the circulation in inflamed parts, namely, *the pressure of the effused transudates* upon the blood-vessels. Thus Glax and Klemensiewicz (No. 12, lxxxiv. III. Ab. Jahrg. 1881, H. 1-5, 1882) have shown that if liquids of different kinds (blood, milk, blood-serum, gum, or salt solutions) be continuously injected through the blood-vessels from the heart, the liquid runs freely enough at first, but there comes a time when it ceases to flow from the venous side. The tissues, when this occurs, have become loaded with liquid, and they hold that it is this which, by compressing the capillaries, occasions the obstruction. The cause of this excessive transudation they believe to be the want of vitality in the vessel wall.

EXUDATION OF LIQUID.

173. An increased transudation of liquid into the tissues is a feature of all inflammations, whether they occur in a vascular or in a non-vascular part. The **bleb** which follows the infliction of a **burn** on the skin, and the **tense feeling** of a part acutely inflamed, as in **erysipelas**, are in great part, an expression of this. The liquid always contains the elements for the formation of fibrin, and hence differs from mere dropsical liquid, in which frequently one of these, the ferment, is absent. It is always poured out under high pressure (Quincke), and hence is a true filtrate. It consequently contains much albumin, much more than natural lymph.

Lassar (No. 13, lxix. p. 516) found, for instance, that when a dog's paw was artificially inflamed, the lymph which ran out of the lymphatics of the limb always contained more solids (chiefly albuminous) than that of the normal limb. The actual quantity of lymph is also greater on the inflamed than on the sound side. Its powers of coagulability, moreover, depend upon the number of cells contained in it.

Dropsy and Inflammation.—*In no case of simple œdema or dropsy* of a cavity *does the amount of albumin in the transudate equal that poured out in inflammation* (Runeberg), and apparently it holds equally true that *the amount of albumin in the most concentrated inflammatory fluid does not come up to that contained in blood plasma.* For the latter reason it has been argued that it cannot have escaped simply through natural or artificial apertures in the vessel wall. There are other factors, however, which serve to influence this result. It is more than probable that it may escape from the vessels both by true filtration through

the wall and by small ruptures of the connective cement between the endothelial plates. We know that hæmorrhages take place in most inflammations, such as croupous pneumonia; and if so, there is no reason why pure blood plasma should not also escape from similar ruptures in the walls. Arnold asserts that he has seen it causing a current in the surrounding parts by streaming out of openings in the wall of the vessel.

THE EXTRUDING FORCE.

174. We have seen that one of the chief and most important phenomena of inflammation is the extrusion of the corpuscular and liquid parts of the blood through the walls of the blood-vessels. What is it that causes these to leave the vessel? In other words, *What is the extruding force?*

Virchow's Attraction Theory.—At the time when the publication of Virchow's works on cellular pathology had inspired all the medical world with a love of the new doctrine, it was held by Virchow himself and by his numerous followers that the essential change in inflamed tissues was located in its fixed elements, and that the participation of the blood-vessels was merely secondary. Thus it was said (see Virchow's numerous works on this subject, *e.g.* No. 13, i. p. 272, iv. p. 261; No. 68, i. p. 46; No. 69, 4 Aufl., Berlin, 1871, pp. 364, 458) that the fixed cells of the inflamed part had an attraction for the contents of the blood-vessels, and tended to draw out of the latter their liquid and solid constituents.

The Amœboid Movement Theory.—When it was discovered that leucocytes escaped through the wall, and that these exhibited amœboid movements, it was immediately concluded that they wandered, by virtue of the latter, through the openings, artificial or natural, presumed to exist in the vessel. How it was, however, that the coloured corpuscles sometimes managed to exude in as great or much greater numbers than the colourless was never explained.

von Recklinghausen, a vigorous upholder of the **amœboid movement theory,** sees no reason to alter his former opinions (No. 81); Lavdowsky (No. 13, xcvii. p. 188) and Binz and his pupils (No. 13, lxxiii. p. 289 (Mees); and lxxxix. p. 389) are still strongly in its favour. The latter seek to justify their opinion by the argument that **quinine,**[1] which is said, although this is disputed by some authors, to paralyse the movements of leucocytes, causes diapedesis to cease. Pekelharing (No. 13, civ. p. 242, 1886) has however shown that the cessation of diapedesis when quinine is administered may be due to quite a different cause, namely, to a hardening of the cement substance of the endothelial plates, which thus lessens the permeability of the vessel wall. Mees (*loc. cit.*) has shown that eucalyptol acts in the same way, and Prudden (No. 82, 1881, p. 82; and 1882, p. 64) and Binz (No. 13, lxxxix. p. 389) have claimed a similar action for salicylic acid and iodoform.

That these substances act by lessening the porosity of the wall seems to be strengthened, according to Pekelharing (*loc. cit.*), by the fact that their administration also diminishes the amount of liquid exuded, as shown by the diminished quantity of lymph carried off from an inflamed part by the lymphatics.

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[1] Consult Scharrenbroich (No. 83), Martin (No. 84), Zahn (No. 85, 1873), Appert (No. 13, lxxi. p. 364), and Kerner (No. 4, vii. p. 122).

The Blood-Pressure as the Extruding Force.—On reflection there cannot remain much doubt that the cause of the extrusion of both kinds of corpuscle is simply **the blood-pressure. Ligature of the artery** effectually puts a stop to it. The column of blood experiences difficulty in being propelled forwards. The energy which ought to have been expended in driving the blood up to the right side of the heart is consequently diverted, and acts deleteriously against the side of the vessel. If there be any small pores or ruptures between the endothelial plates, the soft pliable corpuscles will naturally tend to be adjusted over them, and a continuance of the pressure will force them farther and farther outwards. If, moreover, a stream of liquid be issuing from these pores or ruptures, the corpuscles will be attracted towards them and will incline to be driven outwards. As before mentioned (Sect. 171), the explanation of the leucocytes being at first more abundantly extruded than the coloured corpuscles is probably to be found in the fact that, as the former accumulate in the peripheral zone of the vessel during the slackening in the velocity of the current, they are first applied to the apertures.[1]

As Hering (No. 12, lvii.) has put it, *the whole phenomenon is one of true filtration.* Cohnheim (No. 31, i. p. 238) latterly expressed himself very strongly on this point. "No pressure, no diapedesis," he wrote. It is not necessary that the pressure within the vessel be raised. Indeed there is good cause to believe that it may be diminished.

Experiment.—An experiment for class demonstration, which shows how an obstruction to the flow of liquid through a tube may cause bodies suspended in that liquid to leave it and to pass through its walls, may be made in the following manner :—

Let a tube exactly similar to that shown in Fig. 67 have the lower half of its circumference for a distance of something like ten to twelve inches cut away at a point about one foot from the end. What remains of the circumference of the tube ought to be strengthened with a brass coupling. The whole of the part of the tube from which half of the circumference has been removed is surrounded with stout waterproof tissue, such as the pink jaconet used in antiseptic surgery. The lower part of this is then pierced in many places with a coarse needle.

A mixture of mucilage and gelatine, so thin that it will just solidify, and slightly coloured with carmine, is poured over a sheet of glass and allowed to cool. It is then cut into pieces of about half an inch in diameter. These pieces of coloured gelatine are now introduced in large numbers into the tube through the upright stem, and are allowed to pass along with a slow stream of water, the end of the tube being slightly elevated. So long as the tube is open at its distal extremity, that is to say, so long as there is no obstruction, the pieces of gelatine have little if any tendency to pass through the needle apertures in the membrane, but whenever the exit is obstructed, as by placing a cork in it, the membrane becomes distended, the liquid pours copiously from the apertures, and the pieces of gelatine being attracted to the apertures by the stream of liquid issuing from them, are in the course of a few minutes all extruded. A little bud-like process first forms outside, just as in

[1] This view, taken up by Pekelharing and others, was originally enunciated and experimentally demonstrated by the author (*Proc. Royal Soc. Edinburgh*, Session 1881-82).

the passage of a leucocyte. This gradually gets larger, and finally the whole mass of gelatine makes its way outwards. A suitable glass vessel should be placed below to catch the water and gelatine masses as they issue.

The author is well aware that in many respects such a schematic apparatus does not represent the conditions present in a blood-vessel, manifestly in the fact that there is no provision for diffusing the pressure through collateral channels; but it serves to show in a graphic manner how, if the wall of the vessel be porous from any cause, and if a stream of liquid be issuing from these pores, the corpuscles will tend first to be attracted to them, and ultimately to be driven through.

Literature on Diapedesis of Foreign Bodies introduced into the Circulation.—**Arnstein:** Arch. f. path. Anat., lxi. 1874, p. 494. **Hoffmann and Langerhans:** Arch. f. path. Anat., xlviii. 1869, p. 304. **Hoffmann and v. Recklinghausen:** Centralbl. f. d. med. Wissensch., xxxi. 1867. **Ponfick:** Arch. f. path. Anat., xlviii. 1869, p. 1. **Siebel:** Arch. f. path. Anat., civ. 1886, p. 514. **Slavjansky:** Arch. f. path. Anat., xlviii. 1869, p. 326.

Multiple Embolism a Cause of Inflammation.—As a matter of fact, we know that all the phenomena and results of inflammation may be produced, in the pulmonary vessels at least, simply by a wide-spread obstruction of their terminal branches. Thus it is almost invariable to find some amount of croupous exudation within the air-vesicles in **fat embolism** where the embola are numerous. The lung will sometimes be found to be completely solidified. Now the cause, here, of the croupous exudation must undoubtedly be the obstruction to the onward flow of blood diffusely spread over both lungs by the multiple embola. The embola are bland and unirritating when derived from the medulla of a bone in a case of simple fracture, and hence there could not possibly be a better method of testing the effect, in the pulmonary system of vessels at least, of a wide-spread obstruction.[1]

Croupous Exudations and False Membranes.

175. When the more or less plasmatic inflammatory liquid has been poured out upon a free surface it rapidly coagulates, and the fibrin with the entangled blood corpuscles constitutes what is called a **false membrane**. The fibrin is arranged in dense laminated trabeculæ, in the meshes of which is a finer network of the same, with the extravasated blood corpuscles and any other cells which may have been thrown off from the surface (see Figs. 78 and 79).

In some situations, *e.g.* in the mucous membrane of the larynx or bronchi, the epithelium, uninjured, may frequently be seen underlying the false membrane. Weigert (No. 13, lxx. p. 461) states that, unless the epithelial surface of a mucous membrane be broken, the inflammatory exudation from it will not coagulate. This may be true in a limited sense, namely, that at some part the epithelium may have been broken through, but it is not necessarily broken where the false membrane is deposited. The liquid poured out may subsequently

[1] The relationship of passive congestion to diapedesis is discussed under Dropsy.

find its way over surfaces which are still covered by epithelium. Even on surfaces like the pleura, the delicate endothelium may still sometimes be seen to be preserved.

The liquid of an inflamed part, when infiltrated into the tissues, may coagulate, or it may not. In the **pleuro-pneumonia of oxen** it will be found that the interlobular tissue is filled with precipitated fibrin which has infiltrated into it. In many cases of acute pneumonia in Man, while the air vesicles are plugged with fibrin, the interstitial tissue may remain quite free.

FIG. 78.—ACUTE PLEURISY (×300 DIAMS.)

(*a*, *a*) Network of fibrin; (*b*) an effused leucocyte; (*c*) laminæ of fibrin lying adjacent to the pleura (*f*); (*d*) small round-cells effused into the pleura; (*e*) distended blood-vessels of superficial layer of pleura (Picro-carmine).

The number of leucocytes entangled in false membranes varies. In some of the densest of them there is hardly a leucocyte to be found. Many of the leucocytes, it is said (Schmidt), perish in the act of coagulation.

The **exudation** is poured out in a **liquid form,** and tends to gravitate to the lowest part of a hollow organ like the lung. Hence,

probably, the greater frequency of consolidation at the base of the lung in croupous pneumonia than at the apex.

The false membrane is sometimes called a **croupous exudation,** simply from the fact of its occurring so typically in acute croupous laryngitis. Such false membranes are usually very elastic, but fragile; they can often be stripped off from a part which they cover, such as the pleura, leaving the natural glossy smoothness of the surface.

Their Separation.—All false membranes effused on **mucous surfaces** tend in course of time to separate. The cause of this evidently is that they become undermined by the natural secretion of

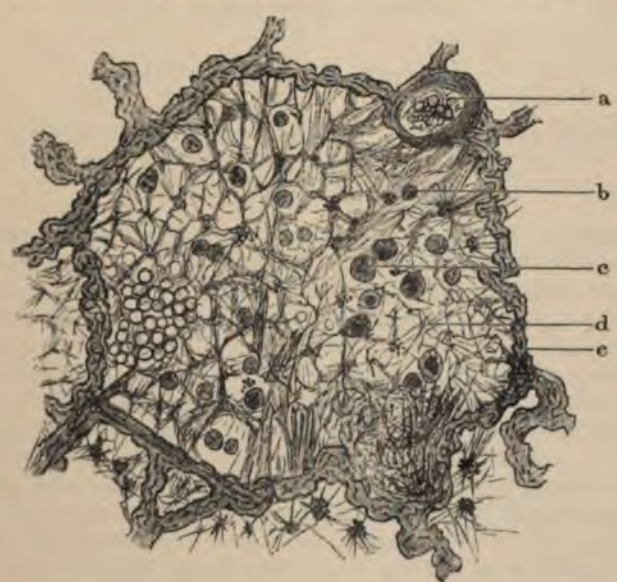

FIG. 79.—ACUTE CROUPOUS PNEUMONIA. AIR-VESICLE FILLED WITH FIBRINOUS LYMPH (×300 DIAMS.)

(*a*) Small artery; (*b*) leucocyte; (*c*) epithelial cell; (*d*) fibrinous network; (*e*) wall of air-vesicle (Hæmatoxylene).

the mucous glands. When, however, the exudation is situated on a **serous membrane,** and especially where it is intermediate between two serous surfaces, it causes these to adhere temporarily simply by its plasticity, and in course of time a permanent fibrous union is brought about (see Sect. 205). At other times, however, the fibrinous network gives way and breaks down, and the effused leucocytes become fatty and also disintegrate. If this occur in a serous cavity it is almost certain to be followed by chronic suppuration of the wall of the cavity; if in a cellular tissue, there is a liability to its ending in abscess; or lastly, the débris may be absorbed.

Literature on Vascular Phenomena of Inflammation.—**Ayres**: Lancet, 1843, ii. p. 102. **Balser** (Method of Observing): Deut. Ztschr. f. Chir., vii. 1876, p. 115. **Broadbent** (Arterial Tension): Brit. Med. Journ., 1883, ii. pp. 357, 363. **Darwin (F.)**: Journ. Anat. and Physiol., x. 1875, p. 1. **Davison**: Lancet, 1882, ii. pp. 884, 933. **Duncan (J. M.), and Gamgee** (Rate of Flow through Tubes): Journ. Anat. and Physiol., v. 1871, p. 150. **Fox**: Brit. Med. Journ., 1881, ii. p. 512. **Goodhart** (Arterial Tension): Brit. Med. Journ., 1885, ii. p. 327. **Kulik**: Ueb. d. Veränderungen d. roth. Blutkorperchen bei entzünd. Processen., 1880. **Löwit** (Examination of Circulation in Warm-blooded Animals): Arch. f. exper. Path. u. Pharmakol., xxiii. 1887, p. 1. **Maragliano** (Blood-letting): Centralbl. f. d. med. Wissensch., xviii. 1880, p. 867. **Norris**: Proc. Roy. Soc., Lond., No. 112, 1869; *also*, On the Laws and Principles Concerned in the Aggregation of Blood-corpuscles, etc. **Ryneck**: Untersuch. a. d. Inst. f. Physiol., u. Histol., in Graz., 1870, p. 103.

CHAPTER XV

INFLAMMATION—(*Continued*)

Changes in the Fixed Tissues. A. Vascular Parts

THE MESENTERY AND OMENTUM.

176. **Structure.**—These membranes may be held to be composed of the following parts. The basis of each consists of bundles of white fibrous tissue with a few elastic fibres, interwoven in such a manner as to produce a more or less fenestrated membrane. Lying upon these bundles of fibrous tissue, just as on all white fibrous tissues, are connective tissue nuclei, corpuscles, or whatever else we may choose to call them. These corpuscles here, and elsewhere, belong to the bundles of fibres, and apparently, when they are separated from them, the bundles suffer in nutrition and are extremely liable to die.

Along with these bundles of fibres are intimately bound up, firstly, arteries and veins, secondly, lymphatic vessels and lymph-canalicular spaces. The lymphatic vessels are composed of a thin endothelial wall, and the lymph-canalicular spaces contain an albuminous fluid which, when stained with gold, looks like a branched cell. It is questionable whether branched cells are to be found in this membrane at all. Finally, each side of the membrane is covered by a single layer of endothelium, in which are minute openings (stomata) communicating with a lymphatic vessel below. The number of lymphatic vessels varies considerably at different parts of the abdominal cavity. They are far more abundant on the under surface of the diaphragm than in any other region.

Method.—If an irritant, such as a piece of worsted thread, be introduced into the abdomen of a narcotised animal (a young dog or guinea-pig is best), and be left there for something like forty-eight to sixty hours, the peritoneum will be found by this time to be in a state of acute inflammation. Its vessels are distended with blood, it has a milky appearance, and a quantity of opaque exudation will be found adhering to its surface. In some parts the opacity will be found to be greater than in others, and these are the foci of most acute inflammation.

Let the animal be killed, and stain the surface of the omentum and mesentery by pouring over it while warm a ½ per cent solution of nitrate of silver. Allow the silver to remain on the membrane until it becomes milky, then cut out portions and wash them in several relays of *distilled* water. On no account put the membrane in ordinary tap water at any time, otherwise the preparation will be damaged; and care should also be taken to change the first washings quickly, to prevent the blood which may have escaped from interfering with the stain. Allow the pieces of membrane to stand in a white basin exposed to bright but not to direct sunlight, and after twenty-four hours mount pieces of them in glycerine jelly (Sect. 45).

The staining must be done immediately after the animal has been killed, otherwise the silver will fail to be precipitated on the borders of the cells.

When the pieces of membrane have become sufficiently brown-coloured (two or three days), the following appearances will be noticed, should the experiment succeed:—

Early Appearances.—We have already seen what occurs in the blood-vessels and their contents. Let us now examine in what respects the fixed elements are influenced. If the inflammation in the part under examination be not very far advanced, and especially, if it be a continuous flat part of the mesentery without meshes, almost the only alteration observable in the fixed tissue elements will be found in the endothelium covering its surface. Instead of its presenting the appearance of a layer of large flat cells, whose outlines are demarcated by the precipitation of the silver, *many of the plates appear to be split into a number of fragments*, whose outlines are blackened by the silver and are thus rendered visible. It is rare for this to prevail over a large area, but it will usually be found that at one part the endothelium on the surface is healthy, while it gradually merges into the broken-up condition just referred to.

FIG. 80.—DESQUAMATING ENDOTHELIAL CELLS OF MESENTERY, YOUNG DOG. ACUTE PERITONITIS (×350 DIAMS., Silver).

The interpretation of this appearance seems to be that the inflammatory liquid effused into the meshes of the membrane has undermined the endothelial plates and has caused them to become loosened. In so doing the delicate body of the cell has been broken up into small fragments.

Endothelial Desquamation.—In many cases the endothelial plate is shed entire, so that the exudation poured into the abdomen in the early stages of peritonitis will be found to contain such desquamated endothelial cells in abundance.

Endothelial Proliferation.—It does not necessarily follow, however, that the whole of the endothelial cells are shed in this way—simply desquamated or broken up without taking any further part in the inflammation. *Their nuclei undoubtedly frequently divide* and give rise to numbers of new cells, which can be seen germinating at particular points on the surface. *These now begin to grow,* and in so doing,

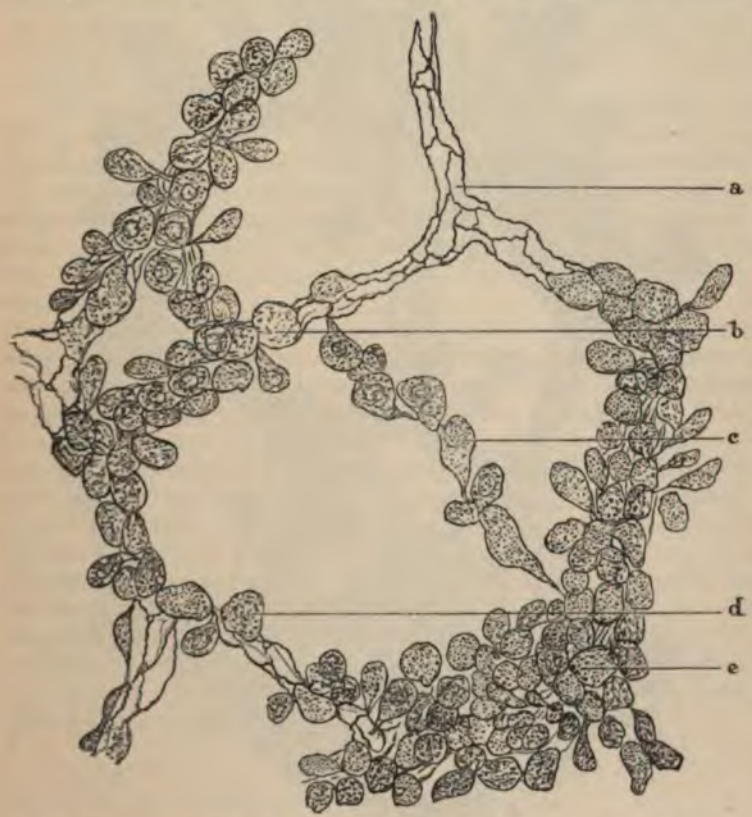

FIG. 81.—GERMINATING ENDOTHELIUM, OMENTUM, YOUNG DOG. ACUTE PERITONITIS (×350 DIAMS.)

(*a*) Natural endothelium covering wall of a mesh; (*b*, *d*) endothelial cells beginning to germinate; (*c*) a chain of germinating cells extending across a fenestra; (*e*) mass of germinating endothelial cells (Silver).

entirely lose the character of endothelial plates. They become round or pear shaped, and contain one large nucleus, or several (Fig. 81).

Connective Tissue Proliferation.—At the same time there cannot be much doubt that *the connective tissue corpuscles assume, in the later stages at least, the same germinal character. From these two sources,* namely, the endothelium covering the surface and the corpuscles lying

on the bundles of white fibrous tissue, *a large proportion of the cellular part of the exudation is derived.*

The appearance accordingly presented, let us say, by a piece of the omentum when the inflammation is just proceeding to suppuration, in the case of the young dog, is the following :—

FIG. 82.—INFLAMED OMENTUM, YOUNG DOG, PROCEEDING TO SUPPURATION (×350 DIAMS.)

(*a*) Germinating endothelial cell sprouting from wall of fenestra ; (*b*) a younger cell of the same kind ; (*c*) the trabecular fibrous tissue on which the germinating cells lie ; (*d*) a mass of such cells thrown off into a fenestra.

Late Appearances.—The blood-vessels have become twisted or bent, and along the course of arteries, veins, and capillaries (Fig. 76) is a dense cellular accumulation, so dense that the course of the vessels is distinctly indicated. The cells are mostly leucocytes, and are of all shapes (Fig. 77). Many of them are pyriform, and are

attached by their tailed end to the wall of the vessel. The peripheral layer of leucocytes within the vessel is sometimes so thick that the coloured corpuscles may be entirely hidden, lying as they do in the axial core.

Among these leucocytes in the immediate vicinity of the vessel, however, are to be found *cells which have nothing in common with them.* They are much larger, and resemble those found on the surface of the membrane. Durante (No. 46, iii. 1871) has described these as in all probability derived from the connective tissue cells of the adventitia.

The endothelium of the surface of the membrane has almost completely vanished (see Fig. 82), by desquamating, either before or after germinating; and instead of the thin lamina of squames to be seen in the natural state, the membrane is now covered with a crop of actively growing cells with large nuclei, often from twice to three times as large as the leucocytes. In the fenestrated parts of the membrane they bud forth in pyriform offshoots (*a*), with a long stem adherent to the fibrous basis.

That these are leucocytes, as is sometimes suggested, seems to be quite untenable. They are so large that if they be compared with the size of some of the capillaries in the neighbourhood, it is perfectly evident that they could never have passed along their channels. They can be kept alive in blood serum, and show amœboid movements. **Threads of Fibrin** are occasionally seen stretching across a fenestra of the membrane, and these large cells become attached to them. The cells also become adherent end to end, thus forming long chains (Fig. 81 C.) This has been suggested as one means by which **adhesions** may be brought about. They are readily separated from the membrane, and are abundantly cast off with the discharge. That they are derived from the endothelium and other fixed tissues is indicated by the fact that they can be seen rising up from the surface of the membrane, gradually enlarging, and finally adopting the pear or pegtop shape which is so characteristic.

PULMONARY EPITHELIUM.

177. In catarrhal pneumonia, an appearance very similar to the sprouting of the cells from the surface of the mesentery is produced by the epithelium of the air vesicles germinating. Large quantities of this germinating epithelium are thrown off into the air vesicles, and are expectorated with the discharge (see "Catarrhal Pneumonia").

MUSCLE.

Waldeyer (No. 13, vol. xxxiv. p. 473), many years ago, showed that the peculiar change which muscle undergoes in **typhoid fever** is

accompanied by proliferation of its nuclei, and he regards the condition more as an inflammation than as a pure degeneration. He confirmed his researches by artificially inflaming muscle in animals. Tschainski of St. Petersburg (No. 70), and Spina (No. 46, 1878, p. 349), have repeated these experiments with similar results.

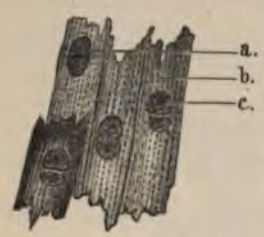

FIG. 83.—INFLAMED MUSCLE, ACUTE MYOCARDITIS (×350 DIAMS.)

(*a*) Enlarged muscle nucleus; (*b*) muscular fibre becoming granular; (*c*) muscle nucleus dividing (Picro-carmine and Farrants' Solution).

In acute **myocarditis** in Man, some beautiful examples of the division of muscle nuclei are occasionally obtained. The sarcous substance becomes very cloudy and granular, loses its striation, and apparently disintegrates. The division which takes place in the nucleus has sometimes been regarded as a sign of **degeneration**. The author cannot agree in this, for while the sarcous substance goes on retrograding and falling to pieces, the essential part played by the nucleus is that of reproduction and growth. It assumes embryonic characters, becomes like the nuclei of the cells in a growing sarcoma, and reproduces itself over and over again. Around it, when liberated from the muscle fibre, there is always a little protoplasm. The nucleus stains deeply with nuclear staining reagents, and in all respects behaves like the nuclei of parts which we know are growing.

The young muscle cells sometimes get mixed up in a **cicatrix** along with the ordinary spindles, and subsequently become developed into striated fibres.

GLAND TISSUE.

178. When the liver is irritated, as by the presence of a foreign body, the liver cells proliferate (Huttenbrenner, No. 70) in the immediate vicinity. In **cirrhosis** of the organ in Man, some of the most beautiful examples of proliferation of the liver cells may sometimes be found (see Cirrhosis).

BRAIN AND SPINAL CORD.

(See Cerebritis and Myelitis.)

CHANGES IN THE FIXED TISSUES. B. NON-VASCULAR PARTS.

179. The **cornea** and **cartilage**, have been much utilised for the study of those phenomena which were supposed to be concerned

purely with the fixed tissues. The former was the battle-ground over which a long controversy was waged between Stricker and Cohnheim, and their respective pupils.

THE CORNEA.

180. Much of the difference of opinion that exists as regards the appearances in artificial keratitis depends upon the various interpretations of its **normal structure**. It is certainly one of the most misleading of all tissues, more especially when stained with silver and gold. When analysed, however, with care, its composition will be found to be comparatively simple, quite corresponding in its essential architecture to that of all the connective tissues.

As is well known, there is a common type upon which the whole of the connective tissues are moulded, and the cornea is no exception to this rule. As we shall see, it is simply a **nucleated fibrous tissue** with a specially free set of lymph channels in place of blood-vessels.[1]

Subject to Surrounding Blood-Vessels.—As previously mentioned, it is somewhat short-sighted to regard the cornea as non-vascular. It is pervaded in every part by lymph channels, and these undoubtedly are in communication with the sclerotic vessels at the border. Hence as the cornea depends for its nourishment on the vessels around it, it must be more or less influenced by the condition of the circulation within them.

181. **Its Structure.**—If the cornea be hardened in Müller's fluid, and a perpendicular section be made through it, it is seen to be composed of **parallel laminæ of fibrous tissue.** These are very numerous,[2] and are so closely bound to each other that they constitute a continuous tough membrane. The only difference between this and any other white fibrous tissue is that a homogeneous **chondrin-yielding cement substance** is infiltrated between its bundles, thereby imparting to the whole mass its necessary transparency. The layers are easily separable after the fresh cornea has been soaked in dilute acetic acid, and if one of these be teased out with needles, it is perfectly evident that each lamina is simply a mass of white fibres[3] (Fig. 84).

The bundles of fibres, however, are arranged in a peculiar way, in so far as those of one layer run almost at right angles to those adjacent, so that in a partial dissection of them they are seen to intercross.

[1] It is impossible to give anything like a *resumé* of the literature of this subject, so ponderous has it become, and the author accordingly has simply referred in the briefest terms to those treatises on its construction which are necessary in order to understand the alterations it suffers when inflamed.

[2] Henle (No. 36, i. 1852) maintained that they were over three hundred in number. It was Bowman who discovered its laminated structure (No. 72, 1845-47).

[3] Consult Rollet (No. 12, xxiii. 1859).

If a coloured fluid insoluble in water, or if mercury (Bowman) be driven in from the border of the cornea, it sometimes accidentally injects the spaces between the bundles and causes the appearance of a number of straight tubes (**Bowman's tubes**) with slight dilatations upon them (see Schweigger-Seidel, No. 73, 1886, and Boddart, No. 50, 1871, p. 22). These so-called tubes are nothing more than the spaces between the rudimentary bundles composing each lamina, and as the bundles intercross, so the spaces or so-called tubes between them similarly intercross.[1]

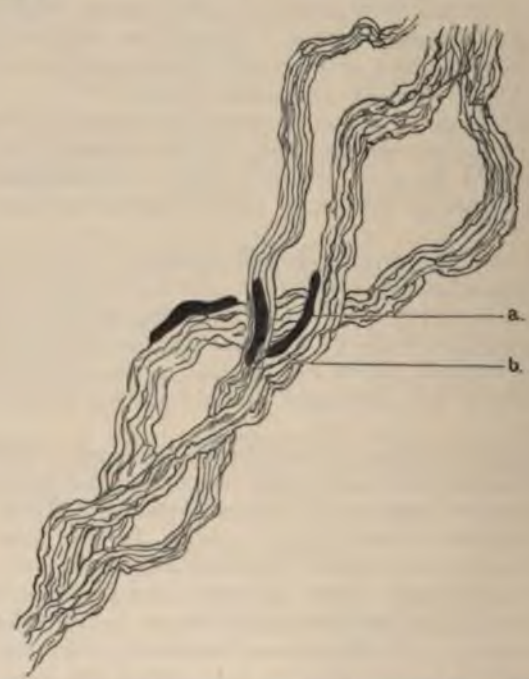

FIG. 84.—BUNDLES OF FIBRES COMPOSING THE LAMINÆ OF FROG'S CORNEA. (Teased preparation. Gold, ×450 DIAMS.)

(*a*) Fusiform nucleus lying on the bundle; (*b*) the bundle of white fibres.

Upon each bundle of fibres lies **a fusiform nucleus** which, if the cornea be stained in gold or hæmatoxylene, can be readily seen when the fibres are separated by teasing (see Fig. 84). When *in situ*, the nucleus is frequently bent or twisted, but when the fibre on which it lies has been separated and slightly stretched, it is found to be closely applied to the bundle and to show a distinctly fusiform shape, like those represented on the bundles of fibrous tissue from a fibrous tumour in

[1] Rollet (No. 75) maintains that they are merely artificial clefts in the fibrillar substance.

Fig. 136. It always stains deeply with gold if the solution has been successful in finding its way into the somewhat impenetrable texture.[1]

Between each two laminæ of the cornea is contained a system of very beautiful **branching plasma spaces or canals**, differing in shape in various animals and anastomosing by numbers of offshoots. In the kitten, at least, and probably in other animals, the wall of these spaces is composed of a distinct **endothelium** (see Hoyer, No. 76,

FIG. 85.—PLASMA SPACES, CORNEA OF KITTEN. (Silver, ×450 DIAMS.)

(*a*) A stellate space; (*b*) intermediate ground substance of lamellæ; (*c*) endothelial plate with oval nucleus lining a plasma space; (*d*) plasma space of adjacent lamina out of focus.

1865, p. 214), each endothelial plate having a delicate **oval or round nucleus** in its centre (Fig. 85), but the finer intercommunicating branches are seemingly made up simply of a cement-like substance.[2] The spaces are, in fact, simply parts of two adjacent laminæ which are

[1] Thin (No. 19, 1875, Part i. p. 398) figures certain delicate spindle cell bodies lying *between* the fibrils of the corneal lamellæ. The author is quite familiar with the appearance, but regards them more as spaces whose contents are stained with gold—in fact, Bowman's tubes.

[2] Rollet (No. 75) states that the endothelium is found only in young animals. With this, however, the author cannot agree.

not adherent, and when seen in cross section, present a fusiform shape, the space being seen on edge.

The nuclei which lie on the bundles of fibres composing the laminæ generally, but not always, correspond to one of these spaces, so that they project into them. As the space is formed by a separation of the laminæ, the bundles composing the latter naturally have to diverge from the continuous plane in which they otherwise run to allow of this. Hence the nucleus which lies on these bundles usually has a bent or twisted appearance when the surface of a lamina is examined. At other times, when the nucleus does not correspond with a space, it appears perfectly straight. The appearance is similar to the distortion which the nucleus of a bundle of fibrous tissue undergoes in **tendon**, only to a less extent.

As to whether the connective tissue corpuscle nucleus projects into the space, or whether it is separated from it and covered by the endothelial wall, it is somewhat difficult to settle. The author is inclined, however, to believe that the connective tissue nucleus does not project actually into the space, but simply shines through its wall, and that the lymph spaces and canals are in reality a set of tubes as completely shut off from the surrounding structure as capillary vessels elsewhere, whose function in some respects they seem indeed here to fulfil.

Branches of the canalicular system run into and at right angles to **adjacent laminæ**, and thus a free anastomosis is brought about between the different systems of spaces and canals.

A **viscid liquid** fills this canalicular system. What the liquid is seems open to question. Were a liquid having a different refractive index from the solid tissues, spread throughout the cornea, it is evident that the function of the membrane would be interfered with. It does not appear to be ordinary lymph, but has a more or less *colloid* character. If it were mere lymph, it would be more readily displaced from the canals after death than it is. It stains with hæmatoxylene, whereas ordinary lymph would not give any such reaction. It is even questionable if the whole of it circulates. It seems more likely that it is an *albuminoid substance* which loosely fills the canals, and thus allows a free circulation of ordinary lymph for the nourishment of the tissue between the two. There is another possibility, namely, that it is simply lymph exuded from the sclerotic vessels at the limbus corneæ, which afterwards becomes concentrated and slowly circulates through the lymph channels. The former view seems the more probable. Lymph corpuscles are frequently carried into the canals and constitute the so-called *wandering cells*, hence showing that the channels are pervious.

Summary.—The cornea is thus composed of laminæ of ordinary white nucleated fibrous tissue, with a system of branching lymph channels and spaces between them. Through these canalicular spaces lymph slowly circulates, carrying with it an occasional lymph corpuscle, and it is by this means that its nourishment is maintained.

GOLD AND SILVER STAINING.

All the difficulties, however, in regard to understanding the cornea have arisen from the peculiar appearances produced by staining it with silver and with gold. Nitrate of silver has the power of staining the outlines of the plasma spaces and canals, while terchloride of gold becomes precipitated on the plasmatic fluid contained within the spaces as well as upon the connective tissue nuclei lying on the bundles, forming with the albumin of the first **an albuminate of gold.**

It will consequently happen that the picture presented by the use of these reagents will differ, for while the silver will bring into view

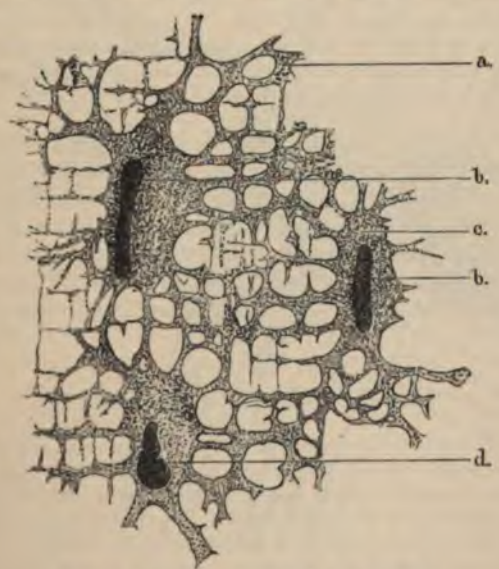

FIG. 88.—CORNEA OF FROG (Gold, × 450 DIAMS.)

(*a*) Branches of so-called cornea corpuscles; (*b*, *b*) nuclei of same; (*c*) a so-called cornea corpuscle; (*d*) a nucleus twisted.

the **walls of the spaces**, the gold will show simply their **contents**. The one picture is that of the walls of the tubes, the other that of the liquid which lies within them.

The silver picture is shown in Fig. 85, the gold picture in Fig. 88. In the former, the endothelial walls (kitten) are distinctly visible, in the latter (frog) these are imperceptible, but a series of branching corpuscle-like bodies is brought into sight.

Against this view,[1] it has been urged that the one often does not correspond in shape to the other. When this happens it is due to two causes, firstly, to the gold

[1] His (No. 74) was the originator of it.

having been imperfectly precipitated on the contents of the finer branches; secondly, to an optical illusion by which the one figure does not seem to correspond to the other. The spaces in the silver figure look wider than the lines in the gold, a purely optical result, as they closely correspond. It will be found, as a matter of fact, that in the **same species** of animals the character of the gold lines coincides with those of the silver, if the staining has been completely successful.

The remarkable point about the gold image is that it looks as if the reagent had brought into view a series of **branching cells** instead of the albuminoid contents of the plasma canals; and this is rendered all the more specious by the fact that in the so-called body

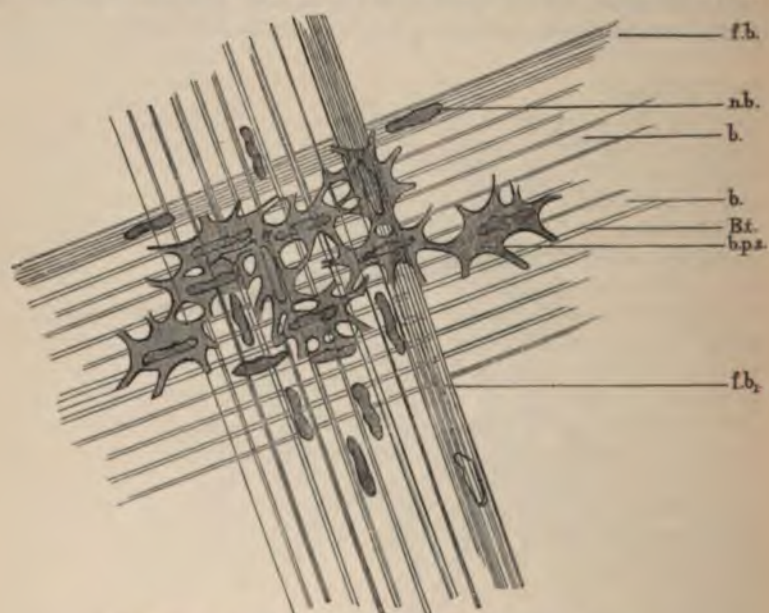

FIG. 89.—DIAGRAMMATIC SCHEME OF STRUCTURE OF GOLD CORNEA.

(*f*, *b*) A bundle of fibres of a lamella divided into its ultimate fibrils; (*f*, b_1), similar bundle of an adjacent lamella running at right angles to former; (*n*, *b*), nucleus of a bundle; (*b*, *b*), similar bundles, the fibrils not represented; (*B*, *t*), Bowman's tubes; (*b*, *p*, *s*), branching plasma spaces enclosed between two laminæ, the nucleus of the bundle shining through them.

of nearly every cell there is to be seen a nucleus. The nucleus is, however, seldom quite centric. It is more often found lying to one side, and has an oblong, bent, or twisted configuration quite unlike the nucleus of any other known cell, unless that of tendon.

These gold stained branching bodies have accordingly been named the **branching or fixed cells of the cornea.**

With Schweigger-Seidel and Thin, the author is satisfied that these bodies are not cells, but that they simply assume this appearance on account of their being composed of an albuminoid liquid moulded in branched canals. If they were true

branched cells, they should be capable of being isolated. Has any one ever succeeded in doing so? What appears to be the nucleus of a branching cell is nothing more than the nucleus attached to a bundle of fibrous tissue entering into the formation of a lamina as before described, and projecting into the space. It is occasionally twisted or distorted from its being applied to the bundle as it circumvents the space, and is rarely perfectly centric.

That this is the correct interpretation of the much discussed nucleus of the so-called branched cornea cell becomes perfectly apparent when the following procedure is adopted. Let a frog's cornea be thoroughly stained in gold terchloride and split into laminæ so as to bring these so-called branching *cells* into view. Lay the corneal lamina on a slide and drag slightly with two needles upon it without at first causing any laceration. Several of the so-called branched cells will be found immediately to vanish, leaving nothing but fusiform deeply stained nuclei lying upon bundles of white fibrous tissue. Pull the tissue thoroughly to pieces with the needles, and not a remnant of a branched cell will be left, but in place of the lovely network previously displayed, the whole structure becomes resolved into bundles of fibrous tissue with large fusiform nuclei adhering to them, undoubtedly the same bodies previously seen projecting into the corneal space (see Fig. 84).

The author, therefore, has little hesitation in concluding (1) that the "branched cells" of the gold cornea do not really exist. They are simply spaces filled with albuminoid fluid. (2) Their so-called nucleus belongs to an underlying bundle of fibrous tissue, and is simply seen through the transparent contents of the space. (3) The reason why the one is seen in connection with the other is that they both stain with gold while the endothelium of the wall of the plasma space does not.

METHOD OF STUDYING KERATITIS.

182. Two of the best corneæ for studying inflammation in are those of the kitten and summer frog. After the animal has been deeply narcotised with chloroform, the centre of the cornea is touched with a sharp point of nitrate of silver, or a thread may be drawn through it. The superfluous nitrate of silver should be neutralised by washing the surface of the cornea with a solution of common salt. In from three hours up to several days, according to circumstances, it should be examined. If it is desired to stain it with nitrate of silver, the animal should be again deeply narcotised and the whole anterior surface of the cornea be rubbed over with solid nitrate of silver (Stricker). The silver stains much more thoroughly when applied *in vivo*, the animal being immediately thereafter killed, or the anterior epithelium may be scraped away, and a 10 per cent solution of nitrate of silver be dropped on to the surface until it becomes milky. In the latter case it should be laid in the silver solution, after being excised, for a few minutes. In both cases, when the staining is complete, the excised cornea must be placed in dilute acetic acid (1 per cent) until it swells up to several times its original thickness. It can be delaminated by the use simply of the scalpel, or it may be cut in the ether freezing microtome, *if care is taken not to over-freeze it.* Two incisions should be made into its margin so as to get it to lie upon the freezing plate. The sections should be mounted in glycerine jelly (Sect. 45).

The same methods of irritation may be employed where it is desirable to stain with gold. The anterior epithelium is scraped off and the cornea excised, the staining being subsequently accomplished by leaving it in a ½ per cent solution of gold terchloride for about half an hour. It is next washed in distilled water and placed

in dilute acetic acid (1 per cent) for twenty-four hours. It ought now to be transferred to a mixture of equal parts glycerine and water, slightly acidulated, and be allowed to remain until it assumes a dark purple colour.

INFLAMMATION OF THE CORNEA.

183. When a cornea is touched in the centre with a pencil of nitrate of silver in the manner just described, the part which is cauterised dies, and shows no evidence of inflammatory reaction. The plasma canals can be seen in it fixed and stained by the silver, but without any of the transformations noticed in those lying farther out. Immediately in contact with its border, there develops, in a few days (see Fig. 90) what is known as the **inner zone of irritation** (His). This area frequently becomes milky and opaque, more particularly when the slough in the centre begins to separate. At a short distance outside of this again is a second opaque ring, the **outer zone of irritation**, more evident than the former, usually constituting a nearly perfect ring, although broader in some parts than others. It is in this outer zone that the inflammatory reaction is most active. In course of time the slough separates and the wound heals.

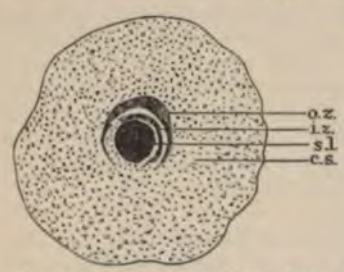

FIG. 90.—SCHEME OF THE PARTS IN ARTIFICIALLY INFLAMED CORNEA.

(*o*, *z*) Outer zone of irritation; (*i*, *z*) inner zone same; (*sl*) slough; (*c*, *s*) remainder of cornea substance.

Cohnheim's Early Views.—If the cornea be irritated by the above means in a frog,[1] and the animal be allowed to live for twenty-four hours in summer, and four to six days in winter, one sees, according to Cohnheim (No. 13, xl. p. 1) the fixed cornea corpuscles in all their pristine beauty, perfectly unaltered. Between or above these, however, are to be found **pus corpuscles** separated or in groups, and sometimes running in straight lines. In the **rabbit** this is virtually also all that is to be made out in most cases. He did not deny, however, that where the irritation is very severe, and where suppuration occurs, the fixed cornea corpuscles become altered. One can see, he said, that in this case the fixed cells become granular, that the processes are contracted, and also that vacuoles may perhaps have formed in their protoplasm. This, however, is a totally different phenomenon from the formation of pus, and will not account for the pus found in suppuration.

To explain the occurrence of pus corpuscles in **suppuration** of the cornea he held that one of two modes of origin must be accepted, either that they have originated in the ever present wandering cells of the cornea, or that they are leucocytes which have passed into the lymph channels of the cornea from the sclerotic vessels at the periphery. In his first work (*loc. cit.*) on inflammation, he stated that keratitis

[1] Eberth (No. 124, and No. 50, 1876, p. 75) states that he believes the appearances following artificial irritation of the cornea differ greatly in mammalia and in frogs. In the former a pure central keratitis results; in the latter it is peripheral in character.

always commenced at the periphery and spread inwards, and that in the early stages pus corpuscles are found more abundantly at the border than at the centre.[1] Curiously the peripheral cloudiness begins at the upper border of the cornea, and only appears at the lower later on. He held the cause of this to be the greater abundance of the blood-vessels above than below.

Coloured Leucocytes.—In order to further prove the identity of the pus corpuscles in the suppurating cornea and the blood leucocytes, he injected finely divided carmine suspended in an acid, or precipitated aniline into the dorsal lymph sacs of frogs; with the result that when he irritated the cornea a few days afterwards, the periphery became coloured from the leucocytes, stained with the particles, which had wandered into it. The particles were not free, but were contained in pus cells.

The Salt Frog.—He abstracted the blood from a frog and substituted salt solution for it. In this state the animal can be kept alive for several days. The cornea was now irritated centrally as before, but no inflammation or suppuration ensued. As Sanderson, however, very properly points out, the conditions of the animal were so altered as in all probability to account for this result. It would be surprising if suppuration did occur.

Suppurative Keratitis—What is it?—The question, however, comes to be, as Stricker puts it: Is this wandering inwards of colourless corpuscles from the margin *suppuration*? Suppuration, he says, is a process by which pus forms, microscopically recognisable pus. Wandering cells in a tissue do not constitute a suppuration. An oculist would never recognise a cloudy cornea as one which was suppurating. This peripheral invasion of wandering cells occurs as a natural phenomenon in many spring frogs. Where we have to do with a veritable suppuration of the cornea the tissue falls to pieces and an abscess cavity results.

Cohnheim's later Views.—Later on (No. 60) Cohnheim's views on the subject of keratitis underwent considerable modification. He recognised that there was a form of keratitis which did not commence at the periphery and spread inwards, but which was central in its origin or at any rate which had its chief seat immediately around the slough. He was considerably exercised to explain how this could be. The following is his account of it:—

First Period.—In gold-stained corneæ of spring frogs, twenty-four hours after central irritation with nitrate of silver, and from eight, ten, to twelve hours afterwards in rabbits, nothing else is noticed in the zone close to the slough than the elements of the part badly stained and in a state of **vacuolation**. Around the slough is a **dark stained line**, and at the outer border of this begin the regular contours of the so-called **cornea corpuscles** with their nuclei. They reach uninterruptedly to the periphery, where, in peripheral keratitis, numerous pus corpuscles are seen lying between them, especially in the anterior lamellæ. As this period closes, however, another commences in which entirely different appearances are found.

Second Period.—The vacuolar figures are paler and with greater difficulty recognised, because they are covered with two kinds of elements; one set is **spicular** and usually thickly set together at different angles; another is composed of the ordinary

[1] Boettcher (No. 13, lviii. p. 362) draws attention to a very important fallacy bearing on this, namely, that with the fewest exceptions, all frogs are affected in April with a peripheral keratitis of a half-moon-like shape.

pus corpuscles, rounded or more commonly **spindle shaped**, only to be distinguished from the spicular bodies by the fact of their containing one or more nuclei which are always wanting in the latter. In **frogs** the spicular bodies are much more frequent than the pus corpuscles, but in the **rabbit** they are not so common. From the commencement these are arranged in rows, and it is curious that they often run at first alongside the nerve fibres. In every case Cohnheim has found the stellate shape of the corpuscles in all zones unaltered, although pus corpuscles may be found lying close by them so thickly as partly to obscure their contours.

In construing the history of these appearances, he said that the spindle-shaped bodies and pus corpuscles clearly, in this case, do not wander in from the vessels of the **periphery.** He has often seen the injection of the border of the cornea and peripheral cloudiness completely fail in keratitis. The explanation of their presence he finds in the fact that the cellular elements of the **conjunctival fluid** are increased, and that these wander into the cornea **through the lesion at the centre.** During the first twenty-four hours the corneal tissue is unbroken, corresponding to the period in which there are few or no pus corpuscles in the part. They cannot gain admittance until the cauterised portion becomes vacuolated and destroyed at the borders and the epithelial covering lost. The conjunctival fluid freely bathes the surrounding parts, and by the action of the eyelids is driven into the canals in the matrix, which become distended and widened. As it mixes with the cementing material or "Kittsubstanz" the more or less spicular figures are produced.

In the normal conjunctival fluid there are always fat, lymph cells, and a small quantity of epithelium. In injury of the cornea the cellular elements of the conjunctival fluid are much increased in number, and these also press forward into the distended interfibrillar channels in a linear manner. Immediately after the separation of the slough the new formation of epithelium commences, the entrance of new corpuscles into the substance of the cornea is prevented, and those which have already wandered inwards spread themselves out towards the periphery.

As may be gathered, Cohnheim *denied that the fixed cornea corpuscles took any part in the formation of pus. He admitted, however, that they are not unchanged*, for while he stated that they do not divide to form new elements, he described the metamorphosis which they undergo as of a retrograde nature by which they become vacuolated and break up into small pieces.

This process of **vacuolation** of the cornea corpuscles has been much dwelt upon by all pathologists who have worked on the subject of keratitis, and has been more especially considered in a very able paper by Professor Axel Key and C. Wallis (No. 13, lv. p. 296). They say that for a considerable distance round the slough the fixed corpuscles become destroyed by this means.

Cohnheim even granted (*loc. cit.*) that in certain instances **divided nuclei** are seen, even in great numbers, within the cornea corpuscles, but asks what signification this has for the fact of their forming isolated individual pus corpuscles. He cannot see that this is a formative process, but would look upon it in much the same light as that **retrograde condition** which Flemming has studied in atrophy of fat cells (No. 13, lii. p. 568; and No. 14, vii. pp. 328, 371).

Seeing, therefore, it is admitted that the so-called fixed cells of the cornea do participate in the suppuration, the whole question of the

production of pus from them rests on whether the parts into which the nuclei divide become in course of time pus corpuscles. On this point Stricker is very clear.

Stricker's Views.—If, he says (No. 31, p. 274), a cat's cornea be irritated in the centre with a point of nitrate of silver and be subsequently stained with silver, the part which has been irritated, when examined microscopically, presents no reaction. The outlines of the network of cornea corpuscles are readily seen but the tissue itself is dead.

Totally otherwise is it in the surroundings. The tissue is thickened, the cell network therein contained is swollen, and its processes retracted; the ground substance or basis of the cornea between the corpuscles is reduced in bulk; the cell network has split into small pieces, and these pieces, when subsequently stained with hæmatoxylene, show a nucleus. The splitting of the cell network occurs at a very early stage in the process. He has found it three hours after irritation, and after twenty-four to forty-eight hours it is present all round the inflamed area. A representation of it is given in Fig. 91, *c*, *c*. He would thus trace the formation of a large number of new nucleated cells to the contraction and subsequent segmentation of the fixed cell network. The parts containing these cells need only to undergo dissolution in order to constitute an abscess sac. The swelling of the cornea, he thinks, is simply the expression of the contraction and swelling of the corpuscles contained in it; it is a phenomenon of growth. The fluid, which he admits is forced into the cornea, may also cause a swelling; not a hard abscess-like nodule, however, but a soft œdematous infiltration.

In interpreting these appearances he starts with what seems to the author to be the erroneous hypothesis (p. 250) that the lymph canals are filled with **cornea corpuscles**, that is to say with protoplasmic bodies in the same way that a hand fills a glove. A cornea which has been bathed in a weak solution of gold, and afterwards in silver, furnishes images like the positive and negative in photography. What Stricker therefore holds by as the interpretation of the foregoing facts is simply that this network of **cells or corpuscles**, which he considers fills the plasma spaces, contracts, divides, and becomes polynucleated, each segment which contains a nucleus forming a pus cell. These in course of time aggregate into masses, and when the tissue softens, are thrown out with the débris of the ground substance as the pus cells of the discharge. In course of time the network is entirely broken up. He does not deny that cells wander in from the periphery, and that these may be coloured as Cohnheim described; but what he holds by is that this does not constitute suppurative keratitis, and is simply a result of the increased flow of lymph.

The points that one would like to be clear about in adopting Stricker's views, are the following:—(1) Are the plasma canals of the cornea lined with endothelium? (2) Are there in addition cells within these canals, or are their contents simply an albuminoid liquid? (3) Are there cells or nuclei upon the bundles of fibrous tissue composing the laminæ of the cornea? If there are these three elements, does each of them divide to form pus? Does, for instance, the endothelium, which composes the walls of the canals, divide, or is it simply this so-called "branched corpuscle" contained within the canal? And, lastly, what is the fate of the fusiform nuclei one can see upon the bundles of fibrous tissue when an ordinary gold preparation is teased out?

Endothelium is in abundance in the very cornea (kitten) which he

has found most suitable in eliciting the segmented condition of the plasma canals (Fig. 91). The author has counted as many as three or four nuclei belonging to a corresponding number of endothelial plates in a single stellate space (see Fig. 85). May it not therefore be, just as we find in ordinary lymphangitis, that the *endothelial* nuclei divide to form part of the new progeny, and that the liquid (not protoplasm) contained in the canals simply escapes?

FIG. 91.—INFLAMED CORNEA, KITTEN (Silver, ×450 DIAMS.)

(*a*) Isolated and nucleated cell; (*b*) a group of such still retaining something of the shape of a plasma canal; (*c*, *e*) plasma canals breaking into fragments; (*d*) the fibrous basis of the lamellæ or the ground substance.

AUTHOR'S CONCLUSIONS.

184. After balancing all the facts of the case, the accompanying history seems in brief to be the true account of what takes place.

Fixed Tissues.—When a cornea is irritated either locally or diffusely almost one of the first things that seems to happen is *an increased flux of liquid into it.* This is poured in through the plasma

canals, and in a few hours comes to distend them. *The canals consequently become swollen*, one of the first phenomena described by Stricker. In course of time, however, this liquid is effused in such quantity, that, just as happens when it is infiltrated under the endothelium of the peritoneum or the epithelium of the air vesicles, *it breaks the endothelial plates into small fragments* (see Fig. 91, *c*, *c*). A large number of the fragments depicted in the dividing network by Stricker contain no nucleus. They are simply dead portions of an endothelial plate. They are small and irregularly shaped, and quite different from the nucleated masses seen lying side by side with them. It naturally

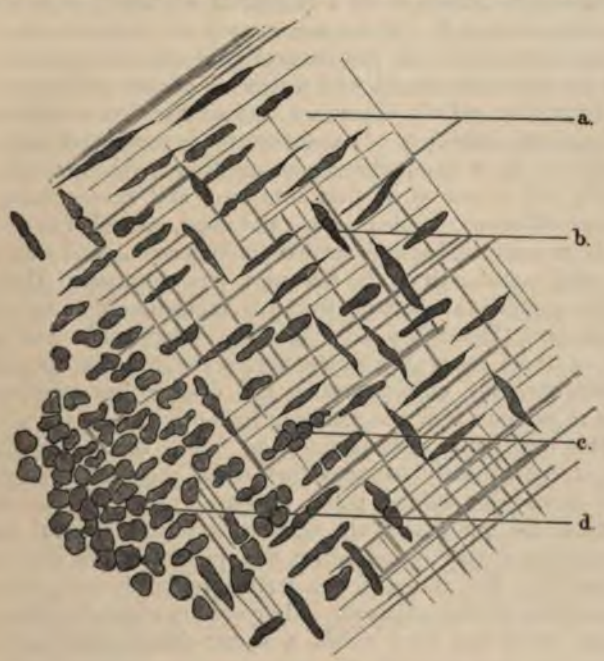

FIG. 92.—INFLAMED CORNEA OF FROG (Gold, ×450 DIAMS.)

(*a*) Fibrous laminæ intercrossing, with their nuclei lying upon them, and all more or less enlarged and prominent; (*b*) a nucleus divided into three; (*c*) a nucleus divided into a little group; (*d*) the edge of the outer zone of irritation, where suppuration is commencing. The branched bodies seen in Fig. 88 had entirely vanished.

happens, as a result of this destruction of the plasma canals, that *the liquid formerly contained in them escapes between two laminæ* and forces them partly asunder. *The so-called branching cells* of the cornea, being nothing more than the liquid contained in the plasma spaces, also *disappear*. It is quite possible, no doubt, that there may be laminæ in which this has not occurred, and these will still show the cell-like aspect. As a matter of fact, however, the branching figures between

the laminæ which are concerned in the active changes, that is to say, in the **outer zone of irritation** round the slough, the part in which pus will shortly appear, have vanished. This may happen in a few hours if the infiltration of liquid has been copious.

The **nuclei** of these destroyed **endothelial plates** do not, however, seem to perish, but, probably on account of the increased supply of liquid pabulum afforded to them, begin to germinate, and in this way the **groups** of new cells found in the inflamed cornea of the kitten are to be accounted for.

When the stellate figures disappear it will be found that opposite where each existed there is left a **fusiform nucleus,** sometimes with a twist or bend upon it. These are simply the nuclei of the bundles of fibrous tissue which in the natural gold cornea are seen shining through the plasmatic liquid, and which are usually called the "nuclei of the branching cells." They are beautifully demonstrable in the inflamed cornea of the frog. If the irritation is continued long enough, they begin to show sympathetic participation in the process. They *divide* (Fig. 92 *b* and *c*) at first into two, and subsequently into a great many oblong or rounded masses, and these, instead of degenerating, as Cohnheim asserted, begin to increase in dimensions, and *form in course of time small round cells* of the size of a pus corpuscle. The area in which this process can best be traced is immediately outside the ring of suppuration (Fig. 90, *o.z*). Here the enlargement and primary division of these connective-tissue nuclei can be seen to perfection, but within the ring of suppuration the division has gone too far to allow us to perceive how the resulting cells originate.

As the bundles of fibrous tissue to which these are affixed run parallel, it consequently happens that when they are enlarging, just previous to division taking place, **rows** of these bodies come into view, and as the bundles of the *different* laminæ concerned run more or less at right angles to each other, the nuclear bodies also appear to intercross (Fig. 92), those of one lamina lying obliquely or at right angles to those of that adjacent. They occupy a spindle-shaped space, and hence what has been called a **spear-head-like** body results. Very soon by their division the spear-head-like bodies vanish, and a little depôt of young cells (*c*), still confined in the same spindle-shaped space but now distended with its cellular contents, results.

Blood-vessels.—Meanwhile, along with the afflux of fluid from the sclerotic vessels, *a large number of lymph corpuscles usually begin to wander inwards,* and these of course tend to accumulate in the part of the cornea where the plasma canals have been broken down, namely, in the ring of inflammation at some little distance from the central slough.

Here, accordingly, they tend to mix with the cells derived from the endothelium of the plasma spaces and connective tissue of the laminæ.

The **fibrous tissue,** finally, within the suppurating area *necroses* on

account of the disturbed nutrition, and an abscess cavity results in which the cells from these various sources are intermingled.

If the irritation be continued for a still longer time (ten days or more), a fringe of vessels arises from the vascular tissues at the border and is pushed into the cornea, in this way constituting a **pannus.**

Sources of the Pus.—The author would therefore plead that the pus in suppurating keratitis is derived from two sources, namely, the **nucleated tissues** of the part and the **blood-vessels** at the periphery; and when we come to contrast it with an inflammation of a vascular part like the mesentery (Sect. 176), it is evident that, non-vascular though the cornea be, there is no *essential* difference between what occurs when it is over-stimulated and that which ensues in the above membrane. Both are made up of the same elements, with the exception of the blood-vessels, but in the cornea the plasma canals are so abundant as in some respects to take their place. We should therefore, *a priori*, expect them to behave in a similar manner, and this seems to be actually borne out by the facts.

CARTILAGE.

185. Hyaline cartilage seems to be a tissue very much like the cornea—at any rate it seems to be built up on the same type. Thin (No. 9, xvi. new series, and No. 149, 1885), by a special method of silvering, has shown that it is laminated; and the basis of these laminæ is a white fibrous tissue. If articular cartilage be examined in the neighbourhood of an ulcerated spot, a complete separation of these fibres and its reversion to an ordinary white fibrous tissue can be readily made out. Redfern (No. 79) showed that when articular cartilage is stimulated or diseased (see also Ogston, No. 5, x.) its corpuscles undergo division and multiplication. The phenomenon is very much like that just described in the connective tissue, nuclei lying on the bundles of fibres in the cornea. Weber (No. 13, xiii.) and Barwell (No. 127) trace the formation of pus to these new cellular productions.

CARDINAL SYMPTOMS OF INFLAMMATION.

186. These are described as PAIN, HEAT, REDNESS, and SWELLING.

That the **pain** is due to the tension of the part caused by the effusion of inflammatory products into it is demonstrated by the almost instantaneous relief that follows from the making of an incision into the affected tissues.

That the **temperature** of an inflamed external part is certainly *higher than the corresponding normal part* on the opposite side of the body can be verified. Thus the one ear of a rabbit inflamed by croton oil is considerably warmer than the opposite (Jacobson, No. 13, li.; Jacobson and Bernhard, No. 50, 1869, p. 289; Laudien, No. 142).

It holds equally good, however, that the temperature of such an inflamed peripheral part is *never higher than that of the general circulation.* It is indeed usually considerably lower than the temperature for instance within the rectum. John Hunter (No. 143, p. 293) was the first to note this from actual observation with the thermometer. He says, "From all the observations and experiments I have made, I do not find that a local inflammation can increase the local heat above the natural heat of the animal, and when in parts whose natural heat is inferior to that which is at the source of the circulation, it does not rise so high." This result is to be explained probably by the increased heat being almost immediately communicated to the system at large, as well as by the loss sustained by radiation from a peripheral part. The ultimate effect is to raise the general temperature of the body. The experiments of Simon (No. 52) and Weber (No. 115, i. Pt. i. p. 381), seemed to show that the temperature of the blood stream returning from an inflamed part was higher than that of the heart. Notwithstanding the care with which these experiments were conducted, subsequent investigators have not been able to confirm them.

The **redness** is due to the increased amount of blood in the part, and the **swelling** to the infiltration of liquid and solid exudation.

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Literature on Tissue Changes in Inflammation.—Consult those given in the text, and:—**Billroth**: Wien. med. Wochnschr., xxiv. 1874, pp. 561-589. **Cornil** (Multiplication of Cells of Bone-Marrow in I.): Arch. de Physiol. norm. and path., x. 1887, p. 46. **Councilman** (Cornea): Journ. Physiol., iii. 1880-81, p. 76; *also*, A Contribution to the Study of Inflammation, etc., 1880. **Ewetzky** (Cartilage): Untersuch a. d. path. Institut. z. Zürich. **Heitzmann**: Allg. Wien. med. Ztng., xix. 1874, p. 133. **James**: Med. Times and Gaz., i. 1867, p. 31. **Kraus** (Epithelial Giant Cells): Arch. f. path. Anat., xcv. 1884, p. 249. **Scheltema**: Deut. med. Wochnschr., xii. 1886, p. 461. **Schottländer** (Division of Endothel. in Inflamed Cornea): Arch. f. mik. Anat., xxxi. 1887-8, p. 426. **Shakespeare**: Med. News, Phila., xl. 1882, p. 481 *et seq.* **Weber** (Cartilage): Arch. f. path. Anat., xiii. 1858, p. 74. **Weigert**: Deut. med. Wochnschr., xii. 1886, p. 482.

Parenchymatous Inflammation.

187. The older meaning of this term was *an inflammation of the substance of an organ as opposed to that of its lining membranes.*

Virchow, however (No. 13, iv. 1852, p. 261), gave it a somewhat different significance. He recognised, for instance, that when a muscle is in a state of parenchymatous inflammation, the primitive bundles become more homogeneous, their striation indistinct, and they break down more easily than usual. Similarly, when the kidney is the seat of it the epithelium of the convoluted tubules becomes swollen, granular, or ultimately fatty. In these cases, he says, there is an

absence of exudation; and the tissue elements are those principally involved. He therefore applied the name to indicate an inflammation accompanied by these tissue changes as opposed to the exudative forms of inflammation met with under other circumstances.

The term, nowadays, has almost entirely fallen into disuse. We now know that the process of inflammation in any part never has the one-sided action attributed to it by the older authors; and that the changes in the tissues constitute simply one of its phenomena. The only sense in which the term is still applicable is when employed to indicate a superficial catarrhal inflammatory affection. The "parenchymatous inflammation of the kidney" is a catarrhal nephritis," and the two terms are constantly employed in an equivalent sense. It is indeed almost the only disease for which the term "parenchymatous inflammation" is still retained

→ *General Literature on Inflammation.*—**Addison**: The Actual Process of Nutrition, etc., 1843 and 1845. **Alison**: Syst. Pract. Med., 1840. **Andral**: Gaz. d. Hôp., ii. 1840, p. 102 *et seq.* **Balfour** (Critique): Med. Press and Circ., iii. 1867. **Beale**: Med. Times and Gaz., 1865, i. p. 593 *et seq.* **Bennett**: Treatise on I., 1844. **Billroth**: Surg. Path., N. Syd. Soc.; *also*, Volkmann's Sammlung klin. Vorträge, No. 4, 1870. **Black**: A Short Inquiry into the Circulation of the Blood, etc., 1825. **Brunton**: Canada Med. Rec., ix. 1880-81, p. 60. **van Buren**: Internat. Encycl. Surg. (Ashhurst), N. Y. i. 1881, p. 65. **Chalvet**: Phys. pathologique de l'Inflammation, 1869. **Cornil** (Production by Jequirity): Semaine Méd., Par., iv. 1884, pp. 29-37. **Councilman** (Keratitis): Journ. Physiol. Camb., iii. 1880-1, p. 76. **Graves**: Lond. Med. Gaz., xxii. 1838, pp. 530-559. **Güterbock**: De Pure et Granulatione, 1837. **Hodgson**: Essay on I., 1829. **Hunter (J.)**: A Treatise on the Blood, Inflammation, and Gun-shot Wounds, 1794. **Jones (T. W.)**: Brit. and For. Med. Rev., xvii. 1844, p. 567; *Ibid.*, xviii. p. 255. **Klebs**: Arch. f. exper. Path. u. Phar., iii. 1875, p. 427. **Meckel**: Ann. des Charité, iv. 1853, p. 218. **Metschnikoff**: Quart. Journ. Mic. Sc., xxiv. 1884, p. 112. **Paget**: Lectures on I., Lond. Med. Gaz., x. 1850, p. 965 *et seq.*; xi. p. 1 *et seq.* **Reinhardt**: Path. anat. Untersuch. 1852, p. 31. **Rokitansky**: Sitzb. d. Wien. Akad. 1854. **Salomonsen and Dirckinck-Holmfeld** (Jequirity Question): Fortschr. d. Med., ii. 1884, p. 617. **Sanderson (B.)**: Brit. Med. Journ., 1882, i. p. 411 *et seq.*; *also*, Rep. Med. Off. Privy Council, Lond., vi. 1875, p. 69; *also*, Med. News, Lond., ii. 1882, p. 75 *et seq.* **Shakespeare**: Med. News, Phil., xl. 1882, p. 481 *et seq.* **Simon**: Holmes's Syst. Surgery, i. 1870, p. 2. **Stricker** (Transl.): Internat. Encycl. Surg. (Ashurst), N. Y., i. 1881, p. 1. **Thoma**: Berl. klin. Wochnschr., xxiii. 1886, pp. 85-103. **Thomson**: Lectures on I., 1813. **Travers**: The Phys. of I. and the Healing Process, 1844. **Valat**: De l'Inflammation considérée comme altérant la cohésion des tissues, 1826. **Virchow**: Archiv. f. path. Anat., iv. 1852, p. 261; Handb. d. Spec. Path., p. 46. **Whittaker**: Louisville Med. News, xi. 1881, p. 182.

CHAPTER XVI

SUPPURATION

188. **Definition.**—We have seen that in inflammation a vast accumulation of cellular and other products takes place in the tissue. Still this does not constitute **suppuration.** The cellular material thus generated may be put to a useful purpose by becoming **organised.** The name literally means **underlying pus** (*sub* and *pus*), and as yet there may be no pus, although the tissue is filled with cells. So-called pus has not always the same histological composition; for, while the usual pus cell is a body about the size of a leucocyte, or larger, containing from one to six or more nuclei (Fig. 93), and more or less fatty, the cells vary in appearance according to the locality. Thus, in a **suppurative peritonitis,** cells twice to three times the size of a leucocyte may be found in abundance, while in a **catarrhal suppuration** the cells, in great part, are unlike those found say in a cellular tissue abscess; and in the pus discharged from a **granulating surface** all manner of cells may be present. Hence the mere occurrence of a particular cell in a tissue cannot be taken as a basis of definition; but it is *the separation from the organism by a natural process of death and degeneration of such inflammatory products as have accumulated within it*, which is the essential point. Once a part has truly *suppurated*, the cells concerned in the process are of no further use for organisation. They must either be absorbed, evacuated, or dry down into a cheesy amorphous mass. Not only the inflammatory products, but the *tissues in which they are contained*, frequently die and are discharged.

FIG. 93.—ORDINARY PUS FROM A WOUND (×450 D., Gentian - Violet, Dammar Lac.)

Causes.—Seeing that mere *inflammatory effusion* is, therefore, not *suppuration*, but that the latter implies the death frequently both of the tissue and its contained elements, how is it that their death is caused?

(1) *Nutritive.*—The usual theory on this subject is that the *surrounding nourishment is insufficient* to support the mass of effusion. It cannot be doubted that this must be a very common cause.

(2) *Micro-Organismal.*—Another factor, however, may go far to explain how the inflammatory products lose their power of organisation and break down to constitute an abscess. Billroth (No. 90) originally showed that acute abscesses contain abundant **micrococci**, and the matter has been more fully gone into by Ogston (No. 6, Mar. 12, 1881). The latter finds that micrococci are present in all **acute abscesses**, and he regards acute inflammation—so acute that suppuration is present or imminent—as always due to these organisms, save in exceptional cases where a burn or a blister may have been at work. Cornil (No. 94, 1883, p. 673; No. 40, 1883, p. 1494; and No. 4, 1884, p. 317) has invariably found in the pus of freshly opened abscesses diplococcus or chains of micrococcus in large quantity.

Of late a number of researches bearing upon this subject have been made on the Continent. The question to settle is in how far the mere application of an irritant is capable of inducing suppuration apart from the occurrence of organismal contamination.

Councilmann (No. 13, xcii. p. 217) was the first to employ the method of introducing irritating substances subcutaneously in hermetically sealed tubes, and after the wound had healed over the tube, breaking it and allowing the contents to escape. He used a mixture of 1 part croton and 5 parts olive oil. He found that a fluctuating abscess resulted, in which he could not discover any micrococcus. By replacing the above liquid with salt solution no suppuration followed, and he consequently inferred, as Orthmann and others had previously demonstrated, that chemical substances such as the above have the inherent property of inducing **purulent inflammation.** This he holds, however, does not exclude what appears to be a fact, that a large number of purulent inflammations in surgery and medicine are due to infectious causes.

Uskoff's experiments (No. 13, lxxxvi. p. 150) and those of Strauss (No. 95, No. ii. 1884) closely correspond in their general bearing with the foregoing. Their results, however, do not appear to have been very constant. With turpentine, for instance, they sometimes obtained suppuration, sometimes not. The latter states that pieces of elder pith and cork never cause suppuration when introduced subcutaneously after being thoroughly disinfected.

Klemperer's results, however, (No. 91, x. p. 158) somewhat differ from these. He finds that the introduction subcutaneously of chemical irritants, such as oil of mustard, petroleum, turpentine, croton oil, and quicksilver, *so long as these have been sterilised*, does not cause suppuration, be they ever so strong. They were confined in sterile glass capsules, and the only effect was the calling forth of a fibrinous effusion which surrounded the remains of the capsule. Similar conclusions have been arrived at by Scheuerlen and Fehleisen (No. 92, xxxii. p. 500); and Ruijs (No. 93, No. xlviii. 1885), experimenting on the anterior chamber of the eye in rabbits, found that substances of this kind did not induce destruction of tissue, but merely a fibrinous effusion without the presence of micrococcus. The latter of these asserts that such powerful irritants induce acute inflammation but no suppuration, and that micro-organisms can cause suppuration possibly by acting chemically. Tillmanns (No. 13, lxxviii. p. 452) repeatedly succeeded in introducing pieces of hardened organs into the abdominal cavity of animals without occasioning peritonitis when strict antiseptic precautions were observed.

This matter, it will therefore be perceived, is still *sub judice*. It is certainly

very questionable whether the micrococci found in abscesses are the invariable cause of the inflammatory effusion suppurating, or whether their presence is in any way more than a mere coincidence. Cheyne has shown (No. 6, Sept. 1884, p. 553) that in a considerable number of cases of wounds which were perfectly free from putrefaction and which were healing without any complication, micrococcus was present in the serous discharge. He explains their not exerting deleterious results by the fact that they belonged to a harmless variety.

The organisms usually met with in connection with suppuration are **staphylococcus pyogenes aureus** and **albus**. They are found in acute unopened abscesses. **Streptococcus pyogenes** is also commonly present together with many more which may or may not be directly related to suppuration. The whole subject, however, is treated at length in vol. ii. under *Vegetable Parasites*, to which the reader is referred for further information.

Proliferation of Leucocytes.—Do the effused leucocytes in a suppurating part *proliferate* after having passed the wall of the vessel? An affirmative answer to this was long strenuously opposed. There seem good grounds for believing, however, from later researches, that, if properly nourished, they may divide, and thus add to the mass of accumulated effusion. It seems very likely that in croupous pneumonia, for instance, a large number of the white cells in the air vesicles are thus to be accounted for.

Catarrhal Suppuration.—See Bronchitis, Gonorrhœa, etc.

Methods of Examining Pus.—(1) Make an ordinary slide and cover-glass preparation.

(2) Examine a drop of pus taken from a cavity or wound, or still better, from the peritoneal cavity while warm on the warm stage (Sect. 59).

(3) Add dilute acetic acid (1 to 3 or 4) to the side of a slide and cover-glass preparation.

(4) Dry a thin film of pus on a cover-slip in the air or in a warm chamber. Draw it three times through the flame of a spirit lamp, and immediately afterwards put a drop of gentian violet solution ($\frac{1}{4}$ per cent in water) on it. Leave the dye on the cover for about a minute, but not longer, and rapidly wash it off in water. Dry the cover and mount in Canada balsam or dammar lac.

This makes a beautiful permanent preparation of the pus corpuscles, their nuclei, and any micro-organisms which may be present.

Literature on Suppuration.—Consult the various text-books on Surgery and Surg. Path., and:—**Apolant**: Arch. f. path. Anat., lix. 1874, p. 299. **Billroth**: Med. Press and Circ., xxxvii. 1884, p. 393. **Brewing** (Chemical Irritants): Diss., Berlin, 1886. **Cheyne** (Report): Brit. Med. Journ., 1884, ii. p. 553. **Cohnheim**: Med. News, Phila., xl. 1882, p. 62. Discussion on Organisms, Wounds, and Inflammatory Transudations, Intern. Med. Cong., Lond., i. 1881, p. 323. **Fehleisen**: Deut. Zeitschr. f. Chir., xiv. 1880, p. 583. **Fraenkel**: Charité Annal., 1885, p. 208. **Fürth**: Studien üb Eiterung u. Entzündung, 1883. **Garrè**: Fortschr. d. Med., iii. 1885, p. 165. **Gostling**: Brit. Med. Journ., 1886, i. p. 112: *also*, Med.-Chir. Trans., Lond., lxix. 1886, p. 183. **Grawitz and De Bary**: Arch. f. path. Anat., cviii. 1887, p. 67. **Jeancon**: Kansas City Med. Rec., iii. 1886, p. 153. **Klemperer** (Relation of Micro-

Organisms to S.): Ztschr. f. klin. Med., x. p. 158. **Lister:** Wien. med. Bl., iv. 1881, p. 1385 *et seq.* **Nepveu:** Cong. franc. de Chir., Proc.-verb., i. 1886, p. 96. **Orthmann** (Causes): Arch. f. path. Anat., xc. 1882, p. 549. **Passet:** Fortschr. d. Med., iii. 1885, pp. 33, 68. **Ringer:** Lancet, 1886, i. p. 107. **Ruijs:** Deut. med. Wochnschr., xi. 1885, p. 225. **Scheuerlen** (Chemical Irritants): Langenbeck's Arch., xxxii. p. 500; *also* (Further Researches), Arch. f. klin. Chir., xxxvi. 1887, p. 925. **Schippers:** Geschiedkundig oversight d. voornamste theorien over onsteking en ettervormig, 1880. **Socin:** Cong. franc. de Chir., Proc.-verb., i. 1885, pp. 103, 251; Rev. d. Chirurg., v. 1885, p. 363. **Strauss:** Compt. rend. Soc. d. Biol., iv. 1883, p. 651. **Stricker:** Wien. med. Bl., v. 1882, pp. 1499, 1531. **Thoma:** Berl. klin. Wochnschr., xxiii. 1886, pp. 85, 103; *also*, Das Problem d. Entzünd, 1886. **Tricomi:** Microorganismi della suppurazione, 1886. **Uskoff** (Does Suppuration exist without Microorganisms?): Arch. f. path. Anat., lxxxvi. 1881, p. 150. **Verneuil** (Orange Colour of Pus): Arch. gén. de méd., cxlvi. 1880, p. 641. **Virchow:** Arch. f. path. Anat., xxiv. 1862, p. 205. **Vogel:** Ueb. Eiter, Eiterung, etc., 1838. **Wagner** (Good Review): Schmidt's Jahrb., ccx. 1886, p. 177. **Zahn:** Zur Lehre v. d. Entzünd. u. Eiterung, 1871.

Literature on Organisms of Wounds and Suppuration.—**Cameron:** Microbes in Fermentation, Putrefaction, and Disease, 1881. **Cheyne** (Micrococci in Wounds, etc.): Brit. Med. J., 1884, ii. p. 553; (Suppuration and Septic Diseases) *Ibid.*, 1888, i. pp. 404, 452, 524. **Cohnheim** (Infectious Causes of Inflammation): Med. News, Phila., xl. 1882, p. 62; (Discussion on Relations of Minute Organisms to Wounds) Trans. Intern. M. Cong., 1881, i. p. 311. **Ernst** (a New Bacillus of Blue Pus): Ztschr. f. Hyg., 1877, ii. p. 369. **Fehleisen** (Inoculation with Abscess Membrane and Fungous Joints): Deut. Ztschr. f. Chirurg., xv. 1881, p. 184; *also* (Etiology), Arch. f. klin. Chir., xxxvi. 1887, p. 966. **Grawitz and de Bary:** Arch. f. path. Anat., cviii., 1887, p. 67. **Hadelich:** Ueb. d. Form u. Grössenverhältnisse d. Staphylococcus pyogenes aureus, 1887. **Horsley** (Septic Bacteria): Rep. Med. Off. Local Gov. Board, 1881, p. 239; (Organisms of Wounds, etc.) Proc. Roy. Med. and Chir. Soc., ix. 1882, p. 167. **Klebs:** Beiträge z. Anat. d. Schusswunden, 1873. **Klein** (Pathogeny of Septic Bacteria): Rep. Med. Off. Local Gov. Board, Suppl., 1882, p. 201; *Ibid.*, 1883, p. 133; (Relations of Septic to Pathogenic Organisms) *Ibid.*, xiii. 1884, p. 133. **Koch:** Ueb. d. Aetiologie d. Wundinfectionskrankheiten, 1878. **Lübbert:** Biologische Spaltpilzuntersuchung. Der Staphylococcus p. aureus u. d. Osteomyelitis-coccus, 1886. **Ogston** (Micrococcus Poisoning): J. Anat. and Physiol., xvi. 1881-2, p. 526; xvii. 1883, p. 24. **Passet** (Micro-organisms of Suppuration): Fortschr. d. Med., iii. 1885, pp. 33, 68. **Wagner** (New Contributions to Cause of Suppuration): Schmidt's Jahrb. ccx. 1886, p. 177.

Fate of the Inflammatory Effusion.

189. (1) **Absorption.**—The liquid effused in inflammation, as proved by Lassar's and other experiments (No. 13, lxix. p. 516, 1877), is removed in great part, if not entirely, by the lymphatics. It often enough happens, however, that the cellular exudation is also absorbed. Even after suppuration has occurred it may happen that the abscess is thus removed along with the broken-down tissue of the part. The greater bulk of the cellular effusion, often amounting to several pounds, may be absorbed in a few days. How is this accomplished?

There are several possibilities—(*a*) The cells may be removed by the lymphatics directly without suffering any retrograde transformation; (*b*) they may similarly be removed by the blood-vessels of the part; (*c*) they may first suffer disintegration, and, after falling to pieces, be removed by the above channels; or (*d*) the dead cells may be devoured by the living.

In regard to the first of these methods, it is only to be supposed,

as the cells find their way into the plasma spaces when they are effused into the tissue, that they should in course of time be transferred to the **lymphatic vessels**. A similar conjecture as to their being carried off by the **veins** when the circulation becomes brisker is supported by the fact that large bodies, such as the pigment corpuscles of the frog's web, have been seen to enter a vessel. Saviotti (No. 50, Nos. x. and xi. 1870) noticed this in the frog's web when the part was acted on by collodion, sulphuric and acetic acids, etc. What the subsequent history of such absorbed inflammatory cells is, remains unknown.

It much more frequently happens, however, that the exudation **disintegrates** before these various channels carry it off. An **emulsion** is formed out of the oil globules resulting from the fatty transformation in which are also suspended fine particles of albuminous débris, and this apparently can be readily absorbed. The process is well illustrated in the resorptive stage of croupous pneumonia.

Phagocyte Theory.—There remains another possible method of absorption which is fast gaining adherents, and on the subject of which more light is now being thrown, namely, that by which the living cells round about the suppurating part carry off and absorb the dead. Lister formerly accounted for the absorption of **cat gut** in a tissue on this theory, and the observations of Metschnikoff seem to lend some support to it. (Consult No. 96, Nos. xxvii. and xxix. 1884; No. 13, xcvi. p. 177; *Idem*, xcvii. p. 502; *Idem*, cvii. p. 209; *Idem*, cix. p. 176; No. 97, T. v. H. 2, p. 141-168; and No. 98, No. xviii. p. 560-565, 1883).

It has long been a matter of mystery how the **larval batrachian tail** becomes absorbed. Metschnikoff explains it on the basis that from the time when the absorption commences one can observe an immense number of amœboid cells in and around the part, in whose interior are pieces of recognisable tissue such as nerve fibre and primitive muscular fibres. These have been intussuscepted by the cells sending out amœboid processes. He calls such tissue-devouring cells **phagocytes**. He believes that the satiated phagocytes enter the abdominal cavity before gaining admission to the lymph and blood-vessels. The pieces of tissue are evidently digested in the protoplasm of the cells. The **gills** are probably removed by the same means.

Another rôle in which they probably take an active part is in the **intussusception and digestion of micro-organisms** circulating in the blood. He noticed that in a parasitical disease to which daphnia is subject the phagocytes seized upon the parasites when they were not too abundant and removed them. When **anthrax bacilli** are introduced into the circulation of cold-blooded animals, and as observed more lately in the case of the **organisms of erysipelas**, the leucocytes show a similar devouring propensity; and hence Metschnikoff regards them as subserving a useful purpose in the economy of the blood by removing noxious particulate matter from it.

If this be so, and there seems good reason to believe that amœboid cells of almost any kind have this property, it might account for the absorption of the **dead tissues** in an inflammatory area, and moreover might explain why a **granulating surface**, that is to say one covered with amœboid cells, is less dangerous as a source of septic contamination than a freshly-made wound.

As bearing upon this, Lister (No. 59, November 19 and 26, 1881, pp. 863, 901) has shown that a blood clot effused into a wound, which is filling with embryonic organising elements, has little tendency to putrefy.

(2) **Caseation.**—Inflammatory effusions in persons with a strumous habit of body have a great tendency after suppurating to dry and caseate. Such may become fertile sources of tuberculosis.

(3) **Organisation.**—(See chapters on Healing.)

Literature on Phygocyte Theory.—**Davis:** Journ. Am. Med. Assoc., Chicago, v. 1885, p. 421. **Hess:** Arch. f. path. Anat., cix. 1887, p. 365; *Ibid.*, cx. 1887, p. 313. **Metschnikoff** (see works cited in text, Sect. 189). **Schäfer** (Digestive Capabilities of Leucocytes): Brit. Med. Journ., 1882, ii. p. 573.

CHAPTER XVII

HEALING OF WOUNDS AND ORGANISATION

190. In his lectures on Surgical Pathology, Sir James Paget describes five methods by which wounds heal, namely, (1) by immediate union; (2) by primary adhesion; (3) by granulation; (4) by secondary adhesion or the union of granulations; and (5) by healing under a scab. From the clinical standpoint this is perfectly true, but when we come to analyse the process more closely, it will be found that all wounds heal in essentially the same manner, namely, *by the growth and organisation of new tissue from corresponding old tissues* already present in the part. The whole process is, strictly speaking, one of *growth followed by organisation*, and any differences which wounds present in bringing this to a successful issue are merely superficial. They may be regarded simply as modifications of the process in its natural simplicity due to certain local causes.

I. Healing by Immediate Union.

191. It is a fact familiar to every one that a clean-cut wound made into a part such as the finger, if kept free from organismal contamination, and if pressure be immediately applied to its edges, will be found adherent in twenty-four hours, and within a day or two, organic union is apparently completed.

If such a wound be examined in about forty-eight hours after its infliction, the only reactionary change will be seen to consist in this, that the **fibrous tissues** and **epithelium** on either side have thrown out a few new cells, and that these cover its interior and surface respectively. The new epithelial cells resemble those of the rete Malpighii, while the new connective-tissue cells are usually at first larger than a leucocyte. The former have been derived from the **old epidermis**, the latter from the neighbouring **connective-tissue corpuscles**. It is only those cells, however, which lie on the edge of the wound that have been drawn upon for this new supply of tissue. The parts beyond are quite unaltered.

There is no **blood clot** in the wound, usually no fibrin, nothing but a little granular albuminous material, which, when it dries on the surface, is the means of closing the wound at first hand.

If such a wound be examined a few days afterwards it will be found that the divided edges of the epidermis have grown together and have rendered the closure complete, while the young connective tissue elements or fibroblasts, deeper down, have united from each side into one continuous layer which is so delicate as to be hardly perceptible to the naked eye, and which, in course of time, can sometimes be traced with difficulty even microscopically. In from ten days to a fortnight, the round-cell character of this layer interposed between the severed edges has become altered. The most of its cells have either a **spindle shape**, or have been transformed into **fibrous tissue**.[1]

Summary.—The wound has healed, and this is the **type** of healing in **all** wounds. It essentially consists in *a growing together* of the two edges by the production of the requisite materials from the old tissues of the part. No blood clot has been interposed between the edges, vascular distension and effusion of blood products have been prevented, and all sources of irritation have been removed. Under such circumstances, *for some unknown reason*, the severed edges tend to *grow* together.

The unusual rapidity noticed in the healing of such a wound is more apparent than real, and is due to the coalescence of the epithelial surfaces a few hours after the wound has been made. The underlying parts do not organise any quicker than in other circumstances, it being always borne in mind, however, that the *quantity* of material to be organised is less than in any other kind of wound.

Literature of Healing by Immediate Union.—**Hamilton (F. H.)**: The art of Primary Union, 1886. **Maurel**: Bull. Gén. d. Thérapie., cix. 1885, p. 121. **Pech**: De la Réunion Immédiate, 1884. **Rushmore**: Proc. Med. Soc. County Kings, Brooklyn, vi. 1881-2, p. 251. **Tourron**: Des Plaies non sanglantes, leur réunion immédiate, 1882. **Verneuil**: Trans. Internat. Med. Cong., Lond., ii. 1881, p. 353.

II. Healing by the First Intention.

192. **Phenomena.**—Where the wound is not so accurately adjusted as in the foregoing and where it is impossible to compress the edges so thoroughly, but where putrefaction and suppuration are excluded, healing takes place by the **first intention**. There is no material difference between this and the foregoing. A little **lymph** or **blood clot** is usually interposed between the cut surfaces which slightly hinders the union, and the cicatrix is also somewhat broader, although still linear in character.

If the surfaces of such a wound be examined in from *eight to ten hours* after the infliction of the injury, they will be found to be covered by a **glossy, sticky liquid**. It may be in such quantity that it soaks the dressings. It consists of a more or less plasmatic transudate

[1] It need hardly be mentioned that the old idea of each divided cell and fibre being brought into such accurate apposition that they again coalesce is utterly untenable.

which has escaped from the divided lymph spaces and blood-vessels. If it dries on the surface of the wound, the albumin contained in it causes the edges to adhere mechanically; and if fibrin, the elements of which it often contains in abundance, be precipitated from it in the depths of the wound, this also tends to mechanically unite the surfaces. If there should be any blood clot in the wound, it may in a manner also aid in holding the surfaces together.

If the surfaces be again examined in from *twenty-four to thirty-six hours*, the glazed appearance will be found to have vanished, and it will be noticed that they have now become coated with a **dull grayish coloured film**.

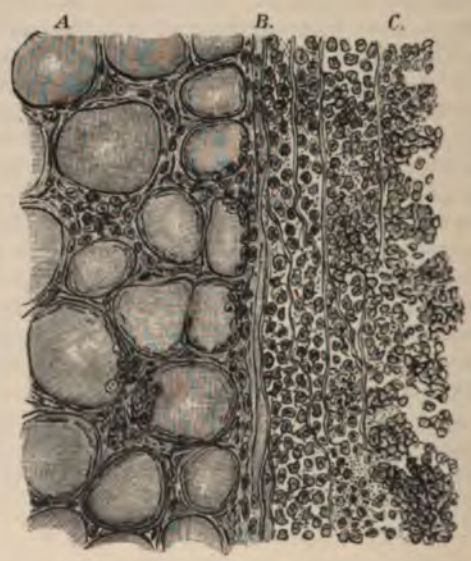

FIG. 94.—HEALING BY FIRST INTENTION. EDGE OF A WOUND FOUR DAYS AFTER ITS INFLICTION. (× 300 DIAMS.)

(*A*) Fat cells with cellular effusion between them; (*B*) edge of severed tissues; (*C*) lymph corpuscles becoming displaced by the small round cells underneath (Picro-carmine and Farrants' Solution).

Microscopically examined this film consists of lymph corpuscles—the corpuscles of the lymph which has escaped from the divided lymph spaces and blood-vessels. These lie in a granular albuminous deposit of precipitated albumin, or, in some places, imbedded in fibrin thrown down from the lymph.

If the two lymph-coated surfaces be now placed in accurate apposition, and if external sources of irritation be avoided, *a temporary adhesion takes place in from forty-eight hours to three days;* and in from *ten days to three weeks or a month* a permanent **cicatrix** has restored the union. How is this accomplished?

Their Explanation.—The lymph which is effused on the surfaces simply subserves a temporary purpose. The wound would heal quicker without it if accurately adjusted. It must be got rid of before the permanent union can take place.

This very soon happens; the **lymph corpuscles** become fatty and disintegrate, and the **fibrinous network**, should such be present, falls to pieces and is absorbed. A similar fate overtakes any **blood clot** which may have been left. These are all unorganisable foreign bodies, and must be got rid of before the advent of true organisation is possible.

From the immediate edge of the wound there grows inwards a layer of **fibroblasts** derived from the divided connective tissues (Fig. 94). The muscular fibres appear to furnish very few of these new elements. Muscular fibre, according to Zahn (No. 13, xcv. 1884, p. 369) regenerates with difficulty even in the fœtus. The **bundles of fibrous tissue** at the immediate edge of the wound are seen to be all actively proliferating. The **nuclei** of their corpuscles are in a state of active multiplication. The new cells thus formed rapidly accumulate around them a cell body, and are removed from the bundle. They then wander inwards towards the free surface of the wound. The **fibrous tissue** from which these have originated, especially if it has been divided, speedily swells, becomes homogeneous, and is apparently absorbed.

The divided **muscular fibres** similarly swell and undergo a colloid-like transformation before being absorbed, so that in course of time the severed tissues present, on either side of the incision, a clean appearance, and are now covered by a layer of *young growing connective tissue* elements.

As these spread further and further into the cavity of the wound they successively *replace the fibrin or blood-clot* which may be present in it, and finally they meet in the middle line and coalesce.

The Blood-vessels.—Meanwhile there has been no unusual vascular distension. The author has been quite unable to see anything like the diagrammatic figures of distended vessels in the edge of the wound given by Billroth (No. 33). Such, if they did exist, would certainly prevent the wound from healing by the first intention. It is well known that parts like the *linea alba* of the abdominal wall heal more readily than those which are possessed of many vessels. The only visible change in the divided vessels is, that they become plugged with a fibrinous clot, while the surrounding capillaries show little increased vascularity. Even in the young cicatrix there are few vessels to be seen, a capillary twig here and there being all that is recognisable. There is no such vascularity as that of a granulating surface. The vessels found in the newly generated tissue are evidently merely sufficient to preserve its nourishment.

The Cicatrix.—In the course of ten days the majority of the new cells have become converted into **spindles**, and in three weeks to a

month a fibrous cicatrix permanently unites the two cut edges of the wound.

Considerable difference of opinion exists as to the manner in which organisation of the spindle cell into fibrous tissue is effected. In the regeneration of tendon Kollmann and Gottschau thought that the new cells simply threw out an intercellular

FIG. 95.—HEALING BY FIRST INTENTION. CICATRIX TEN DAYS OLD, LINEA ALBA, OVARIOTOMY (× 50 DIAMS.)

(a) Neighbouring epidermis; (b) corium continuous with cicatrix (c); (e, e) neighbouring tissues; (d) united epidermis; (f) portion of same included in cicatrix; (g) fat cells in side of wound. (Hæmatoxylene and Farrants' Solution).

substance, and that this subsequently became fibrillated. This view has been more and more losing ground of late years, the majority of observers (Schwann, M. Schultze, Cohnheim, Leydig, Semper), being now convinced that the processes of the cell actually split into the fibres. Ziegler (No. 110), Tillmanns (No. 13, lxxviii. p. 437), Beltzow (No. 14, xxii. p. 714, 1883), Hamann (No. 100, xxxix. Pt. i. p. 145, and *idem*, p. 309), and Ginsburg (No. 13, lxxxviii. p. 263), are quite clear about the latter

view, and the author's experience coincides with theirs. The spindles assume a more and more attenuated character; their tapering ends become pale and evidently undergo some transformation by which they are converted into a structureless substance. This splits longwise into the fibrils of the future bundle, while the original nucleus, with apparently a little of the body of the cell, remains flatly adherent to the bundle as its connective-tissue corpuscle.

Ziegler (*loc. cit.*), and Tillmanns (*loc. cit.*), although coinciding in this method of formation of connective-tissue fibres from cells, trace the origin of at least part of these cells to **leucocytes** escaped from the vessels, the latter, exclusively, to this source. It is a remarkable fact pointed out by Virchow that since the discovery of diapedesis nearly every round cell lying in the tissues has been called a leucocyte. How, for instance, Tillmanns can call the cells he depicts (quite accurately) in Fig. 10, pl. ix. (*loc. cit.*), *leucocytes*, the author cannot conceive.

Cohnheim (No. 31, i. p. 29), in writing on organisation of inflammatory products, stated that it is certain that all development of cicatricial tissues is dependent upon large **epithelioid cells** (fibroblasts ?). The more rounded of them, by virtue of their sending out processes, become spindle and stellate in shape. The processes grow and become further metamorphosed, chiefly in that they split and are so converted into fine fibres and fibrils. From each end of a spindle cell there is thrown out a pencil of delicate wavy attenuated fibres. The broad side of the cell may also give rise to fibres which develop out of its protoplasm. These large epithelioid cells, however, he traced to **colourless blood corpuscles**. He agreed (p. 285) with Ziegler that the one leucocyte may devour the other and so become *enlarged*, and also that by over-nourishment the cells may become converted into **giant cells**. If this be true one cannot exactly see why, when they are immersed in the richest of all nourishing fluids, the blood, they should not similarly grow into giant cells.

The **epithelium** unites in exactly the same way as in healing by immediate union.

Summary.—The union of the wound, therefore, in healing by the first intention is brought about by the reproduction of new connective tissue and epithelium from the old tissues of the like kind. These, as pointed out by Fraise in a recent essay on the subject (No. 101), and as generally admitted in pathological new formations, regenerate themselves more readily than any other tissues. What the cause of their regeneration may be, however, is as yet obscure. As Fraise remarks (*loc. cit.*), neither the irritation of wounding, nor an increased supply of nourishment (Thiersch), nor the withdrawal of opposition to growth (Boll) alone can account for it.

Method.—The study of healing by the first intention is perhaps better carried out in Man than in any of the lower animals, and chiefly for this reason that the wound can be kept perfectly aseptic and pressure be more accurately applied than in an animal. In connection with every large hospital there is always plenty of suitable material to be had either from the dead subject or in parts which have been removed from the living for various causes while healing is going on.

In studying the process in the lower animals, the author has found that those with a thick derma are most suitable. The wound should be made in a part containing as little subcutaneous fat as possible, and where the animal cannot gnaw the dressings. The strictest antiseptic precautions are to be enforced. The skin must be shaved widely around the part, and be thoroughly cleansed first with soap and water, subsequently with carbolic lotion (1 to 40). The incision should be made under the

spray, and the wound be dressed with a collodion styptic containing a large percentage of boracic acid and sterilised cotton fibre. This should be dropped on until a tumour-like elevation is built up, the animal being kept narcotised until it is dry. Bandages are always difficult of application in small animals, and even in those which are larger they often are the means of causing the wound to putrefy. The great object to be aimed at is to excite as little reaction in the tissues as possible, otherwise the process is sure to be complicated by vascular distension and its concomitant evils.

Harden in "C" for three weeks, subsequently in "A" for a fortnight. Put the parts while warm, or as soon as possible after death, in the hardening solution. Imbed the wound in celloidin before it is cut if it happen to be of recent date, having previously removed with alcohol and ether as much of the subcutaneous fat as possible. This, if abundant, materially interferes with its proper examination. Stain in hæmatoxylene and mount in Farrants' solution. For demonstrating the general appearance of the cicatrix with a low power, the preparation may be clarified in oil of cloves and mounted in dammar lac.

III. Healing by the Second Intention, or Granulation.

193. When a wound is left exposed, and when accurate pressure is not applied to its edges, it begins to granulate. Vascular tufts are thrown out on the raw surface, and a discharge more or less purulent is cast off from it. The wound in such a case heals from the edge inwards.

The parts to be seen in it are the following:—

(1) *The granulating surface in the centre.*

(2) *A bluish-pink pellicle at the margin.*

(3) *The blanched cicatrised part beyond this continuous with the sound tissue.*

(1) **The Granulating Surface**—A. *Its Superficial or Vascular Layer.*—The basis of each tuft of granulations is a bunch of capillary loops. Each loop takes its origin from a small **artery** and enters a corresponding **vein**, or there may be a common stem which arises from the artery, and which subsequently breaks up into secondary and tertiary branches which finally become united in a vein. Sometimes a loop arises at one end from a small artery, and *re-enters it* at a little distance further on. The **walls** of the capillaries resemble those of natural vessels; the nuclei of their endothelial plates being usually remarkably large. The loops are wider at their curve than elsewhere. They contain a considerable number of coloured corpuscles, and always a disproportionately large number of **leucocytes**. In the immediate vicinity of the **loops** many leucocytes tend to accumulate, and these are pressed out on the free surface as one of the elements of the discharge.

The loops sprout upwards in bunches, and it is these which give the papilla-like shape to the granulations. In a wound typically healing by the second intention the granulations are always particularly *small*—mere vascular buds.

Round about the capillary loops is a delicate open-meshed and œdematous **stroma,** and upon its bundles of fibres may be seen numerous connective-tissue corpuscles, all more or less germinating. It is attached to the walls of the vessels, and gives them support. Within its meshes are contained the **granulation cells.** These are of two kinds, namely, small round cells, *leucocytes,* derived from the distended loops, and cells two or three times larger, *fibroblasts,*

FIG. 96.—HEALING BY SECOND INTENTION. PERPENDICULAR SECTION THROUGH EDGE OF HEALTHY GRANULATING WOUND, OLD ULCER OF LEG (×50 DIAMS.)

(*a*) The discharge; (*b*) the bluish-pink pellicle of young epidermis; (*c*) older epidermis; (*d* granulation tissue; (*e*) injected blood-vessels; (*f*) deep organising layer beneath cicatrix; (f_1) same beneath granulations (Hæmatoxylene and Farrants' Solution).

derived from the neighbouring connective tissues. Sometimes a third cellular element is added, *giant cells,* but this is not a constant constituent. They appear to be simply overgrown fibroblasts (see Sect. 200). The fibroblasts are usually round, sometimes branched.

B. *Its deep Cicatrising Layer.*—In a healing wound the depth of the granulating surface is very slight, not more than an eighth of an inch. Beneath it, in all such healing wounds, there is a **cicatrising layer,** composed of the same elements as a young cicatrix in a wound healing

by the first intention, namely, round and spindle-shaped cells with, it may be, some newly-formed fibrous tissue. It is more fibrous towards the edge of the wound than at its centre.

(2) **The Bluish-pink Pellicle.**—The delicate pellicle of tissue seen at the edge of all wounds healing by the second intention represents the young epidermis which is about to cover in the exposed surface.

FIG. 97.—GRANULATION TISSUE FROM WOUND REPRESENTED IN FIG. 96. BLOOD-VESSELS INJECTED (×400 DIAMS.)

(*a*,*a*) Capillary loops with several branches; (*b*) ordinary granulation cells; (*c*) fibroblast; (*d*) stroma (Hæmatoxylene and Farrants' Solution).

The new epidermic cells are generated from the old, and, as they accumulate, they are pushed inwards, firstly into the depressions around the granulations, and subsequently over them.

It should be mentioned that Rindfleisch (No. 102), Golding-Bird (No. 63, 1879), and others supposed that the new epithelium was generated from the granulation cells. This idea is now abandoned by every one. It would be such a revulsion of

all our notions of embryological order and predestination that one cannot entertain it for an instant.

The most important literature on the subject of formation of new epithelium will be found in the following treatises :—

In reference to the regeneration of the cornea epithelium: Wadsworth and Eberth (No. 13, li.), Hoffmann (*ibid.*), Heiberg (No. 46, 1871), and Wyss (No. 13, lxix. 1877) should be consulted. Klebs (No. 104, iii. 1875) has an article on the regeneration of epithelium in the frog's web; while Heller (No. 105, p. 28) showed the new epithelium to be regenerated from the old at the edge of a wound in the frog's tongue. Griffini (No. 49, i. 1884, p. 53) has confirmed what the author previously recorded on the regeneration of tracheal and bronchial epithelium when it has been shed by inflammation (No. 103), namely, that the new cells arise from stray cells which have been left upon the mucous membrane. Hennum (No. 49, i. 1884, p. 56), and Fraise (*loc. cit.*), hold similar views as regards the regeneration of new epithelium from the old; while Pfitzner (No. 13, vol. ciii. p. 256, 1886) has lately shown that a short way from the edge of the wound a zone of epidermic cells with karyomitotic figures may be recognised.

The cells at the extreme edge of the epithelial pellicle have a more or less rounded shape. They closely resemble those found in the rete Malpighii. At first they do not readily adhere to the underlying surface, but in course of time seem to throw down long **processes,** which pierce into the tissue beneath, and in this way take hold of it. The epidermis eventually develops precisely the same layers as in the natural skin.

The granulations at the edge of the wound previous to the young epidermis spreading over them become very much reduced in size, and before the new epidermis will form a proper attachment all unorganisable granulation cells and vascular distension must disappear. The leucocytes rapidly vanish, and the fibroblasts, as the granulations become reduced in size, are converted into spindles of the young cicatrix. So long as the granulation basis is in a congested and œdematous condition there is little tendency for the epidermis to cover it. The young cells are apparently undermined by the œdematous fluid, and are thrown off as soon as they are generated. The granulations being thus removed, the **deep** or **cicatricial layer** which, as described, underlies them, is exposed, and it is in reality over *this* that the epidermis spreads.

Reverdin's discovery of **skin grafting** (No. 106, No. xiii. Dec. 1869; No. 6, 1870; and No. 107, 1872) proves the power of transplanted epidermis to reproduce itself. **Islands** of epidermis frequently arise in the midst of granulating wounds. Their presence is to be explained, not upon the theory of a transformation of the cells of the granulations, but rather from the fact of some epithelial remnants having been left on the surface during the process of ulceration which may have occasioned the wound. Schweninger (No. 108) showed that **hairs** could similarly be transferred to a granulating surface. Masse (No. 109, 2d serie, T. iv. No. 1, pp. 1-32) has transplanted them into the anterior chamber of the eye. Bert failed to do so; but Masse states that it is necessary to remove a portion of the epidermic sheath to insure success.

Reconstruction of Papillæ.—When a wound heals by the **first** intention, papillæ are absent from the cicatrix even although it be broad. When, however, the healing is effected by the **second** intention, true papillæ reform upon the epidermis. In the latter case the granulation loops atrophy downwards and become the papillary vessels. The construction of papillæ seems to be dependent upon these vessels.

Literature on Skin-grafting.—**Dickinson**: St. Louis Med. and Surg. Journ., xlv. 1883, p. 105. **Girdner** (fr. Dead Subject): Med. Rec., N. Y., xx. 1881, p. 119. **Monod**: Gaz. d. hôp., liv. 1881, p. 700. **M'Carthy**: Med. Press and Circ., xxx. 1881, p. 311. **Petersen** (fr. Frog): Vrach, vi. 1885, p. 541. **Reverdin**: Soc. de Chirurgie, xiii. 1869; *also*, Archiv. gén. de méd., 1872. **Turnbull**: Trans. Am. Med. Assoc., Phila., xxxi. 1880, p. 869.

(3) **The Cicatrised Area.**—When the edge has become covered with epidermis, organisation of the embryonic elements rapidly takes place, followed by the production of fibrous tissue. All remaining vascular dilatation vanishes, a cicatrix has been formed, and the healing is completed.

The Discharge.—From the vascular loops, as previously described, many **leucocytes** escape, and the larger and more tortuous the former are, the greater the number that seem to be capable of passing through their walls. Along with them, a more or less highly **albuminous liquid** exudes. Many of the **fibroblasts** of the granulations are also cast off, and these three elements, present in varying quantity, together constitute the discharge. As they are generated, they tend to be pressed out in the direction of least resistance, that is to say, on to the surface of the wound.

Flabby granulations are such as have very wide and long capillary loops, and whose open meshed reticulum is distended with œdematous liquid.

FORMATION OF GRANULATIONS AND NEW BLOOD-VESSELS.

194. It is usually supposed that the capillary loops thrown up upon an exposed surface are newly formed. Blood-vessels are newly formed no doubt under certain physiological and pathological conditions.

Arnold (No. 13, vol. liii. p. 70; and liv. pp. 1 and 408) has described the process very carefully in the regenerating **tail** of the frog tadpole, in the **cornea** in artifically-produced panophthalmitis, and in the **vitreous humour**. The method by which the new vessels in these situations are regenerated is, according to him, that from the endothelial cells of the wall of a pre-existing vessel a **protoplasmic mass** is shot outwards, which continues to grow by throwing out processes terminating in thread-like extremities. These become converted into **loops** by their terminations uniting. The protoplasmic processes are afterwards hollowed out into **tubes** and suffer subsequent dilatation, while nuclei begin to appear in their wall. The at first continuous

and homogeneous or faintly granular wall next becomes subdivided into **endothelial plates,** each with a nucleus, and so a new capillary is generated. The new vessels are invariably capillary in character. They may afterwards become surrounded by an adventitious sheath.

Ziegler (No. 110 and No. 50, October 28, 1876) has practically confirmed this description, but like Brodowski, he also traces their embryonic connection with **giant cells,** at least in many cases. Several wandering cells become incorporated into one protoplasmic mass or giant cell. From this mass a few processes are projected outwards. These unite with rows of spindle-shaped cells linearly arranged, and so a network results. Protoplasmic sprouts are thrown off from neighbouring vessels which unite with this network. The whole network of cells and fibres subsequently becomes hollowed out, commencing at the offshoot from the blood-vessel, with the result that in course of time a branching system of new vessels follows.

Billroth (No. 111) describes *three* methods in his well-known essay by which blood-vessels are developed in the **embryo.** The **first** of these consists in the laying down of solid cylinder-forming cells closely united together. These subsequently become hollow and their contents are transformed into blood corpuscles which are afterwards carried into the circulation. The walls of the new vessels he supposes are composed of the cell membrane.

The **second** differs from the first, in that rows of spindle cells with processes lie in close apposition. They enclose spaces between them, and these become transformed in time into the channels of the vessels. Thiersch's researches (No. 115, B. i. Ab. 2, H. 2) practically coincide with this view.

The **third** corresponds closely with the method described by Arnold, namely, that the vessel wall sends out thread-like projections which unite with similar offshoots, or with processes of branched cells, or directly with another vessel. The processes subsequently become hollow and are thus converted into blood-vessels. New cells develop in their walls.[1]

Granted that these various methods of blood-vessel new formation are capable of verification in pathological and embryonic tissues, the question comes to be: Are the vascular loops which spring up on the exposed surface of a wound to be traced to similar modes of origin? Are they not merely the superficial vessels of the part which have become distended with blood and partially detached from the tissues in which they lie? Ziegler (*loc. cit.*) has stated that the vessels of granulations pass through the same transformation in developing as those of other parts. The evidence on which this rests, however, is meagre.

The process of granulation formation in Man the author finds to be the following:—If the exposed wound be examined in about forty-eight hours after it has been inflicted, the superficial, lacerated, or divided dead tissues will be seen to be in a state of disintegration, and shortly afterwards they begin to separate from those which are still living. The most superficial capillaries at the same time undergo a remarkable alteration. They are converted into huge sac-like cavities, filled to distension with blood (see Fig. 98). Every small capillary

[1] Other papers have been published on this subject. The following should be consulted:—Ranvier (No. 18), Carmalt and Stricker (No. 46, 1871), and Schäfer (No. 112 xi.)

which otherwise would have remained unnoticed, has been rendered a prominent object from the excess of blood which it contains. Shortly afterwards, they become tortuous and have a tendency to bulge upwards or rather outwards on the free surface.

Examined a few days later, it will be found that these same vessels have been projected still further outwards, and now are recognisable as granulation loops. Round about them is a dense layer of leucocytes. The whole process seems to be one of distension and displacement of superficial capillary vessels naturally present in the part. —See author's paper on "Healing" (No. 5, xiii.) and "Sponge Grafting" (No. 19, November 1881).

FIG. 98.—SUPERFICIAL CAPILLARIES OF A WOUND BEGINNING TO GRANULATE, ABOUT FORTY-EIGHT HOURS AFTER ITS INFLICTION (×350 DIAMS.)

(*a*) Free surface; (*b*) the capillary loops all distended with blood, and being driven outwards in tortuous festoons; (*c*) young granulation cells (Picro-carmine and Farrants' Solution).

As the vessels are thrown upwards they carry with them a little areolar tissue. This becomes œdematous from the infiltration of liquid, and constitutes the **stroma** of the granulations.

Cause of Vessels being Displaced.—All the liquids and tissues of the body are under a certain **pressure**. The expulsive action of the heart, opposed by the elasticity of the tissues, strikes a balance at a certain mean. Under such circumstances a **cavity**, in the strict sense of the term, whose walls are not rigid is a physical impossibility. All the so-called cavities, such as the peritoneum, pleura, or pericardium, must necessarily either have their surfaces in accurate apposition or must be filled with some resistant material which will

counterbalance the pressure of the blood on their various sides. If a separation were to occur between the surfaces of the pericardium, the pleura, or the peritoneum, the immediate effect would be to cause transudation of liquid into it from the blood-vessels until the pressure in the cavity became equal to that of the blood-vessels ramifying in its walls; or, if this were prevented, the **capillary loops** on either side of the cavity, not meeting with sufficient support from the mutual pressure of the two walls, would tend to be pushed inwards so as to fill the vacuity.

Every capillary in the body has a tendency to be pushed further and further outwards from the heart as a pumping centre, as may be explained by the accompanying scheme.

Let L (see Fig. 99) represent the left side of the heart, and R the right. The blood, leaving the left ventricle by the aorta (A), will be diverted from running in a straight line only in so far as it is opposed by certain forces. In completing the circulation it is so acted upon by these forces that it runs back through the vena cava (V C) in exactly an opposite direction from that in which it passes down the aorta (A). The opposing force which determines this entire change in the direction of the blood-stream is to be found in the walls of the blood-vessels; for if we suppose *c*, *c*, *c* to represent capillaries, it is evident that it is by their intervention that the reversal of the stream occurs.

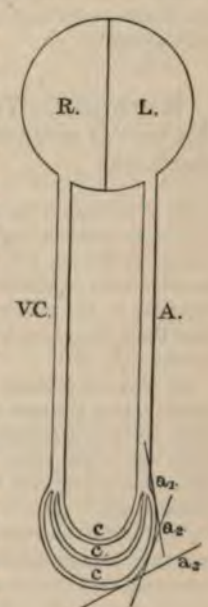

FIG. 99.

Now, it is apparent, that, as the blood would, practically speaking, continue to run in a straight line unless it were for the intervention of the curved blood-vessels, the stream must impinge against the coat of the vessel at points a^1, a^2, a^3, and will tend to drive the vessel outwards and to straighten it. That this displacement does not actually occur is the result of the resistance of the fasciæ and skin, which so bind the capillaries down in their places that eversion is prevented. In the case of a cavity, such displacement is prevented by the mutual compression of the various sides.

Landerer (No. 113), evidently in ignorance of the author's work on this subject (*loc. cit.*), has propounded exactly the same doctrine, and has founded a theory of inflammation upon it (No. 114, No. cclix.) In the former of these works he says that the tissues, owing to their elastic properties and the tension of their fluids, must react on the circulation of the blood through them. If, for example, the pressure within the capillaries of the brain be accepted as equal to 300 mm. of water, and the tension of the cerebro-spinal fluid be equivalent to 200 mm., it is evident that only one-third of the blood pressure is borne by the capillary wall while two-thirds must have

been expended upon the tissues. By a number of ingenious experiments he has formed an approximate estimate of the counterpoise afforded by the tissues in Man and in the lower animals. In a powerful man he found it to be equivalent to a pressure of 550 to 600 mm. water, about three-fourths of the conjectured capillary pressure under the skull (v. Kries). In the subcutaneous tissues of the rabbit he found it to be equivalent to 15-30-60 mm. water, and in the dog's skin it came up to 140 mm. He holds that the surrounding tissues act upon the capillaries in the same way as the elastic coat of an artery acts upon the blood within it. The amount of resistance, however, varies according to the co-efficient of elasticity of the part, and according as the capillaries are surrounded by liquid or by solid tissue. In **œdematous tissues** there always is a perceptible extensibility and incompleteness in their elasticity. This, along with alterations in the vessel wall, he holds to be the cause of œdema. The loss of elasticity may be the result of long-continued stretching. The tissues thus normally act as an **elastic cushion** opposed to the pressure of the blood from within. In **inflammation** he believes that this elasticity and resistance are lost from the part being injured, and hence the vessels become dilated and engorged.

Examples.—There are many facts which prove that a restraint of this kind is required in order to prevent capillary distension and displacement:

(1) If we remove the **skin** and leave the part exposed, the almost immediate effect is that the surface begins to granulate; and if we study how these granulation vessels are formed, it is evident, as just described, that they are nothing more than the superficial capillaries of the subcutaneous tissues which have been displaced and elongated by the pressure of the blood within them. There is no evidence to show that these blood-vessels are newly formed. The loops can be seen in all stages of eversion.

(2) Make an **incision** into a tissue, bring the edges together so as to exert mutual pressure, keep the part free from irritation, and the two injured surfaces will rapidly unite without granulating. Expose the surfaces of such a wound by separating them, and do not apply any counter-pressure, and the whole of the superficial capillary loops, which have lost the restraining influence of the tissues, will be everted as granulations.

(3) There is no tendency to granulation on the **pleural** or **peritoneal surfaces** or on the **mucous membrane** of the **bladder**. Separate the adjacent surfaces, however, and they will begin to granulate like the surface of a fresh wound. The granulating mucous membrane of the extroverted bladder is a good example of this.

(4) The vessels of the **brain** are restrained in their position by the resistance of the cranial vault and membranes. Remove these resisting media, and the brain is seen to pulsate in the first instance, and, if it becomes at all inflamed, is forced out in the form of a hernia.

(5) The granulations in a varicose **ulcer of the leg** are larger when the limb is dependent, because there is more than ordinary pressure exerted upon them by the weight of the whole blood column. The tendency to ulceration on the leg is simply an expression of the effects of increased pressure upon the resisting skin. In order to relieve this pressure and to avoid ulceration, we raise the limb and place the patient in the recumbent position. The cause of the ulceration is that the balance which naturally exists throughout the whole body between the expulsive action of the heart and the resistance of the tissues has been disturbed and is in favour of the former. The undue capillary tension must be removed by counter pressure or by

raising the limb before the balance can be again struck between the expelling force and the resistance. If, on the other hand, an unduly great amount of contracting cicatricial tissue should result after healing is complete, the balance between the two may be again disturbed, in an opposite direction, and a shrinking of the limb follow.

Amount of Discharge in Relation to Position.—The distended capillary walls in a granulating wound, like those in an inflamed part, are more porous than naturally, and readily allow the exodus of liquid and blood corpuscles. The coloured blood corpuscles escape in small number, because they never come near the wall, but run in the axis as before explained (Chap. xiv.) The leucocytes catching in the bends of the vessel tend to be applied over the pores, and hence are extruded by preference. The extruding force is the blood pressure, and the greater this is, the more liquid and leucocytes will be expressed. Hence the **position** of the part on which a granulating wound is situated will have a marked influence in increasing or diminishing the amount of discharge thrown off, and also in regulating the size of the granulations. This quite coincides with the everyday experience that if a person suffering from an ulcer of the leg walk about, the discharge increases in quantity, the granulations become exuberant and œdematous, and the wound does not tend to close. These effects are in great part counteracted by keeping the limb horizontal.

INFLUENCE OF GRANULATIONS IN THE HEALING OF A WOUND.

195. An exposed wound will heal without granulating *provided that the superficial vessels are kept in their places by accurately applied pressure, and that all flux of blood into them is averted by the wound being preserved free from putrefaction and inflammation.* The statement can be verified daily in the practice of antiseptic surgery. The wound becomes covered with a **grey pellicle** of new tissue elements, and the epithelium spreads over this as a surface, without there being any more vascularity than is necessary for organisation.

Lister has frequently drawn attention to this. The wound in course of time contracts and heals in a much shorter time than if a rich crop of granulations had been forced outwards on its surface.

When superficial parts of the cornea are excised, the wound heals quicker than in any other situation (Wyss, No. 13, lxix.; and Gütterbock, No. 13, l.), and it is effected simply by the embryonic epithelium rapidly filling up the wound. There are no blood-vessels to hinder its progress.

When it is desired to favour the healing of a granulating wound, every possible appliance is adopted for the purpose of *getting rid* of the granulations. Pressure is

taken off their capillary loops by raising the limb; counter pressure is applied to them by strapping, bandages, weights, etc.; or they may have to be destroyed by some corrosive, or by the actual cautery. Every means is taken by the surgeon to *curtail* them, knowing that as long as they are exuberant healing cannot take place. The amount of vascularity requisite to favour healing is just such as will afford sufficient nourishment to allow of organisation. Any exudation of blood products over and above this is simply so much nourishment wasted, and is naturally thrown off from the free surface. When the epithelium is about to spread over the surface the granulations have practically disappeared as before described (Sect. 193).

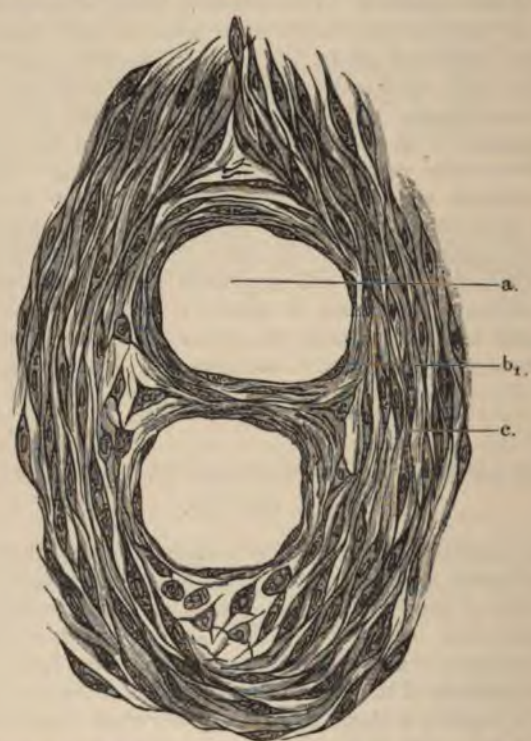

FIG. 100.—HORIZONTAL SECTION THROUGH DEEP OR CICATRISING LAYER OF A GRANULATING WOUND (×400 DIAMS.)
(*a*) Capillary stems of granulation loops cut across; (*b*) endothelium of same; (*c*) spindle-cell tissue surrounding them (Picro-carmine and Farrants' Solution).

Natural Atrophy of the Granulations.—It is therefore evident that instead of granulations being *always* a provision of Nature to aid in organising the exposed surface, they are rather the unavoidable outcome of the peculiar circumstances in which the part is placed, and they may be the very means by which healing is retarded.

So much is this recognised, as it were, in the spontaneous healing of the wound, that a **natural provision** has been made for their

destruction. Attention has already been drawn (Sect. 193) to the fact that, underlying the granulations, there is a *layer of cicatrix-like elements*, mostly spindle-shaped cells. As the stems of the granulation vessels are projected upwards they have of course to run through this layer, so that, in a horizontal view, it is seen to be perforated by them (Fig. 100).

When the process of healing is going on, this layer of cicatrix-like elements begins to contract, and, in so doing, constricts the capillary stems passing through it, thus bringing about a natural atrophy of the granulation loops.

Of course, the author would not be interpreted as meaning, that granulations *never* under any conditions subserve a useful function. They are often the means by which the elements of organisation are carried into a part (see Chap. xviii.), and under ordinary circumstances a *moderate* amount of vascularity is beneficial to organisation. Where, however, the granulations are at all *exuberant*, they act distinctly in a deleterious manner in furnishing more organisable material than can be utilised, all that is necessary in order to enable the wound to heal being a thin layer of young cicatrix elements. Over this the epidermis always tends to spread ; its cells apparently can take hold of it and obtain a firm footing. They can not do so, so long as the divided tissues alone form the surface of the wound.

Action of Stimulants.—The beneficial influence of stimulants locally applied, such as a blister, solutions of various salts, etc., in causing an indolent ulcer to heal, is probably to be accounted for by the substance acting upon this young connective tissue layer beneath the granulations. They most likely induce its cells to proliferate, and thus bring about the construction of a suitable surface over which the epithelium may spread.

Method.—Far the best examples of healing by the second intention are to be obtained from Man in limbs and other parts which have been amputated. The part should instanteously be plunged *entire* into "E" for forty-eight hours. The wound should next be cut out and transferred to "C" for three weeks, and to "A" for a fortnight. The tissue does not require to be embedded, but is simply cut in the freezer. Stain in hæmatoxylene if a general view of the parts is desired, and in safranin if the nuclear plexus in the epithelial cells is to be the special object of observation. The former is best obtained in a perpendicular section, the latter in one made horizontally. Mount in Farrants' solution or clarify and mount in dammar lac. The limb may often advantageously be injected.

IV. Healing by Secondary Adhesion.

196. When two granulating surfaces, as for instance the exposed flaps after an amputation, are placed in apposition, they unite if undue suppuration is prevented. The manner in which this takes place is the following—

The mutual pressure of the flaps very soon constrains the granulation loops and causes them to atrophy. This brings the two deep, cicatricial, or organising layers into contact, and they then simply

grow together by an interlacing of their spindles in a manner identical with that which occurs in healing by the first intention. The process, therefore, simply consists in the *destruction of the granulations* and the consequent *apposition of the two fibroblastic surfaces.*

V. Healing under a Scab.

197. There is nothing special in this, further than that the scab (dried liquor sanguinis and epidermis) affords a convenient protection to the exposed surface, and prevents the access of deleterious particles which might fall upon it and cause putrefaction.

SUMMARY OF FACTS RELATING TO THE FIVE METHODS OF HEALING.

198. We have seen that in healing by **immediate union** and by the **first intention,** the process essentially consists in the growth of a wall of new tissue from the tissues at each side of the wound. It is composed chiefly of young fibroblasts. Over this, epithelium will spread, provided it is not too vascular, so as to complete the reparation of the lesion. In healing by **granulation,** the exuberant granulations must be removed either spontaneously or by artificial means; and when the deep or cicatricial layer underlying these is exposed, the epidermis covers it just as it spreads over the young cicatrix resulting from healing by the first intention. There is no difference in the two processes further than that the extent of cicatrix to be "epidermidised," if one may be allowed such an expression, is greater in the one than in the other. In the one there are at first two layers of cicatricial tissue; these subsequently unite. In the other there is only a single layer from the commncement. The nature of the process, however, is alike in both, and consists in the growth of an **embryonic connective tissue basis,** over which the epidermis subsequently diffuses itself. Why epidermic cells should thus tend to run superficially has never been explained.

The other two methods are of course simply modifications of these. All other phenomena, such as **excessive granulation, suppuration,** etc., are **complications,** not essentials of the process.

General Literature on Healing by First and Second Intentions.—**Bennett** (in Old Persons): Brit. Med. Journ., 1884, i. p. 1144. **Gamgee:** Trans. Intern. Med. Cong., Lond., ii. 1881, p 493. **Humphry** (in Old Persons): Brit. Med. Journ., 1884, ii. p. 55; *also*, Journ. Anat. and Physiol., xix. 1884-5, p. 115. **Kocher:** Volkmann's Sammlung klin. Vorträge, No. 203-4, 1882. **Leloir** (Nerves of Vegetations): Compt. rend. Soc. de Biol., v. 1880, p. 228. **Nolberg:** Berl. klin. Wochnschr., xvii. 1880, p. 668.

CHAPTER XVIII

HEALING OF WOUNDS AND ORGANISATION—(*Continued*)

Organisation of Porous Dead Materials.

199. When a porous substance of any kind is placed in contact with a vascular surface, its pores speedily become filled with organising tissue and blood-vessels, and in course of time it becomes incorporated with and, if of suitable dimensions, buried in the tissues.

Numbers of different porous substances have been employed. Thus Heidenhain (No. 116), who was the first to make experiments of this kind, used **elder pith**; Rustizky (No. 13, lix.), pieces of **glass** and **bone**; and Ziegler (No. 110), two **cover-slips** cemented together in such a way as to leave a narrow space between them; Baumgarten (No. 13, lxxxii. and lxxxvi.) studied the process in **silk ligatures** and other foreign bodies; Zielonko (No. 50, No. lvi. 1873) and Tillmanns (No. 13, lxxviii. p. 437), in **dead pieces of tissue** such as liver, lung, and cornea; while Senftleben (No. 13, lxxvii.) employed **blood-vessels** taken from different animals. The author's own experiments were made with **sponge** (No. 19, 1881), and Marchand (No. 13, xciii. p. 518) has repeated and confirmed these. Balls of **worsted**, the **swim-bladder** of the fish, etc., have also been put to a similar purpose. The majority of the experiments consisted in placing these substances in the abdominal cavity or in the subcutaneous cellular tissue.

Method.—Whatever the substance selected may be, it should first be thoroughly sterilised by prolonged soaking in carbolic acid solution (1 to 40), and the operation should be performed with strict antiseptic precautions. As even a small quantity of carbolic acid acts as a violent poison to many of the lower animals, the tissue to be introduced should be freed from it as much as possible. Harden the part for three weeks in "C," subsequently for a fortnight in "A"; cut in the freezer; stain in hæmatoxylene or picro-carmine; and mount in Farrants' solution.

TURKEY SPONGE.

200. From its extreme porosity this is one of the most useful substances for experimenting with. It is built up of a set of branching

FIG. 101.—SECTION THROUGH THE BORDER OF A PIECE OF SPONGE PLACED IN ABDOMINAL CAVITY FOR TEN DAYS. IT HAD BECOME ADHERENT TO THE BOWEL (×300 DIAMS.)

(*a*) Stem of large swollen capillary vessel running upwards from the intestine; (*b*) loop of same; (*e*, *e*, e_1) pieces of sponge, the last with a capillary loop (*d*) coiling round it; (*e*, *e*) part of the sponge filled with fibrinous lymph; (*f*, *g*) layer of round and spindle-shaped fibroblasts piercing (*i*, *i*) into the part of the sponge (*e*, *e*) filled with fibrinous lymph; (*h*) a blood corpuscle.

fibres composed of **keratode** on which the sponge **protoplasm** lies during life. The framework alone is left when the sponge is dried. These fibres interlace in all directions, thus constituting the ingoing and outcoming channels. It can be easily adapted to a part of irregular shape, and can be readily rendered aseptic.

When a small piece of a porous body such as sponge is placed with antiseptic precautions in the abdomen of an animal, it need *not* excite general peritonitis. It generally becomes attached to a coil of intestine within a few days, and in *ten days* will be found to have become so firmly adherent to the peritoneal coat that it cannot be separated without tearing the latter. If it be incised, a layer of organising tissue from $\frac{1}{8}$ to $\frac{1}{10}$ inch deep will be seen by this time to have penetrated into its substance. Similar phenomena are found to follow when the sponge is applied to a fresh wound or placed on a granulating surface. The manner in which this organisation is accomplished is the following:—

The first thing noticed is that *the interstices of the sponge become infiltrated with blood-stained fibrinous lymph.* The incurrent and excurrent canals do not usually become occluded by it, but a fibrinous network is found adhering to their walls with many leucocytes entangled in it.

In course of time, however, the sponge *becomes invaded by a layer of true fibroblasts* of round and spindle shape. These progressively push their way inwards, supplanting the fibrinous lymph which had taken possession of the sponge network in the first instance. At the point where the two meet, the fibrin can be seen falling to pieces (Fig. 101 *e*, *e*) and becoming absorbed, and it is quite possible that the new cells live upon it. The only cells contained in the fibrinous lymph are leucocytes (*h*), or, at any rate, cells identical with them in shape, size, and delicacy of outline. These *leucocytes* rapidly fall to pieces, they are consumed along with the fibrin, *and take no part in the permanent organisation.* The cells which succeed them are mostly larger than a leucocyte, some of them several times the size (*f*, *g*). They have a much more decided outline, and are possessed of one or more large nuclei. They are usually round in shape when young, but all rapidly tend to become converted into spindles.

Their origin is self-evident. We have supposed the sponge in the present case to have become adherent to the bowel. The active changes which have occurred in the bowel at the point of adhesion appear to be concentrated in the **peritoneal coat** and **subperitoneal connective tissue.** The muscular and mucous coats show very little participation, further than in the fact of the connective tissue proliferating here and there between the bundles of the former.

The bundles of fibrous tissue of the peritoneum and those immediately underlying it will be found to have become loosened and opened out, so that the peritoneum is no longer recognisable as a distinct membrane. The connective tissue cells lying on these bundles have all been thrown into a state of activity; they have become enlarged,

and division is rapidly proceeding within them. The endothelium of the part, more especially that of the surface of the peritoneum and of its lymph vessels, appears to be implicated in this reaction. That of the peritoneum soon vanishes as well as the sharp border which ought to be distinctive of the peritoneal boundary line.

From these proliferating sources, *a vast number of new cells soon arise, which accumulate upon and within the coats of the intestine, and make their way into the sponge framework.* As they do so, the spindles of which they in great part consist, twine themselves round the branches of the framework, and, tendril-like, give support to the delicate blood-vessels, in this way aiding in the efficient nourishment of the new tissue.

Vascularisation.—The vascularisation of this *organising layer* of tissue elements proceeds *pari passu* with its spreading into the sponge. The following will be found to be the manner in which it is effected :—

The vessels of the peritoneum and those immediately subjacent first become dilated and engorged with blood. Every small ultimate capillary becomes a huge varicose trunk. They next show a peculiar tendency to become tortuous, and the tortuous parts incline to be displaced from their natural position. As the disintegration of the tissue just described goes on contemporaneously, these tortuous vessels are pushed more and more outwards towards the free surface, and are naturally carried up, surrounded with fibroblasts, into the interstices of the sponge. Long stems are seen reaching from the intestinal wall into the sponge as far as the free border of the organising layer, where they form most beautiful capillary loops.

Within from ten days to a fortnight, at the end of which time vessels are to be seen everywhere throughout the new tissue, the author has been unable to detect the formation of new vessels by the budding process. He feels strongly persuaded that up to this time the vessels which are projected into the sponge along with the organising elements are not newly formed, but are simply the vessels of the intestinal wall elongated and dilated. It is quite possible, although positive evidence is wanting on the subject, that, later on, new vessels are thrown out in the form of buds; but the first means by which the new tissue becomes vascularised is alike with that by which the granulation vessels arise upon an abraded surface (see Sect. 194).

Comparatively few **leucocytes** are to be found around them. Deeply within the intestinal wall, where the vessels are just becoming tortuous, it occasionally happens that leucocytes are seen in process of passing through the wall, but only exceptionally and in localised areas. The retardation of the flow of blood through the new vessels, necessary for the exudation of leucocytes, evidently does not exist. It is not as in an inflamed part. There is very good reason for believing that the circulation through them has been unusually brisk. Those trunks which lead up from the intestine possess a distinct adventitious coat,

and have all the appearance of having existed long before the process of organisation commenced.

Organising Layer.—The constitution of this **organising layer** is, therefore, identical with that of the corresponding layer seen deeply in a wound healing by the second intention. In course of time it spreads through the whole sponge, and, issuing on the surface, completely covers it in. The epidermis, if the sponge be placed in an open wound, runs over this easily, seeing that the latter possesses the

FIG. 102.—SMALL PIECE OF SPONGE FROM THE WOUND CAUSED IN EXCISING THE MAMMA (×350 DIAMS.)

(*a*) Sponge framework; (*b*) giant cells; (*c*) fibro-blasts (Picro-carmine and Farrants' Solution).

properties which, as we know, in other localities (Sect. 193) permit of this occurring.

Presence of Giant Cells.—Lying among the young cicatricial elements of this organising layer are numerous giant cells. They are in close contiguity with the sponge framework, and in most cases are adherent to it (Fig. 102). They are occasionally of enormous size, and contain abundant nuclei. In some cases they are very numerous, so that clusters of them are seen adhering, amœba-like, to the keratode branches.

Their mode of origin in granulating wounds and elsewhere has been much studied of late years.

Lange (No. 117, 1874) and Thoma (No. 13, lxv.) came to the conclusion that in **lupus** nodules they were formed by an aggregation and fusion of smaller cells. Arnold (No. 13, lxxxii.; No. 13, lxxxvii., and No. 13, lxxxviii.), Gaule (No. 13, lxix.), Waldstein (No. 13, lxxxv.), and Kiener (No. 4, 1880), believed, from the study of **tubercle**, that the giant cells there are also formed in this way. Klein (No. 118, Part ii.) found that in the tubercular lung they result either from overgrowth of individual epithelial cells or from the fusion together of several smaller cells. He rather favours the latter view.

Lange (No. 13, lxv.) also studied their formation in **blood** effused into the lymph sac of the frog, Weiss (No. 13, lxviii.), in **foreign bodies** introduced into the tissues, Aufrecht (No. 50, 1877), in **bone**, and Tillmanns (No. 13, lxxviii.), in **pieces of dead animal tissue** placed in the abdomen; and likewise inferred that they were the effect of a fusion of smaller cells. Schüppel (No. 126, 1868, H. 6) believed that those found in tubercle arose from a confluence of leucocytes within blood-vessels. On the other hand, Virchow (No. 35, ii.), Loven (No. 119, 1873, iv.), Herrenkohl (No. 120), Friedländer (No. 13, lxviii.), Baumgarten (No. 50, 1876 and 1878; and No. 13, lxxxii. and lxxxvi.), Lübimow (No. 13, lxxv.), Flemming (No. 13, vol. lxxvii.), and Marchand (No. 13, vol. xciii.), studying them in different situations, concluded that they were the result of the enlargement of a single cell, followed by division of its nucleus into the nuclei of the giant cell. Ziegler (No. 121) and Cohnheim (No. 31) held the same view, but regarded the cell out of which the giant cell is developed as a leucocyte which becomes inordinately large by devouring its neighbours. Others, such as Langhans (No. 13, xlii.), Rustizky (No. 13, lix.), and Klein (*loc. cit.*), regard both methods of formation as possible.

In reference to the source of the cells out of which the giant cells grow, there are chiefly two views—(1) That they are originally extravasated leucocytes (Ziegler, *loc. cit.*; Jacobson, No. 13, lxv.; Aufrecht, *loc. cit.*; Lange, *loc. cit.*; Senftleben, No. 13, lxxii. and lxxvii.; Tillmanns, *loc. cit.*) (2) That they are formed from the fixed cells of the tissues, such as connective tissue corpuscles (Weiss, *loc. cit.*) or endothelium (Rindfleisch, No. 122, xiii. 1879; Wagner, No. 123; Baumgarten, *loc. cit.*; Klebs, No. 13, xliv.; Köster, No. 13, xlviii.; and Marchand No. 13, xciii.). Other varieties of fixed cell have been alleged to give rise to them, such as epithelium; while osteoblasts are a fertile source of them in tumours and other diseased conditions of bone. Brodowski (No. 13, lxiii.) described them as connected to a newly formed offshoot from a small blood-vessel, and as being converted, in course of time, by a process of vacuolation into new vessels. He looks upon them as "hypertrophied angeio-plastic cords." Rabl (No. 50, September 9, 1876) traces them to enlarged lymph cells and fibroblasts.

Appearances which look very much like a fusion of small cells to form those of giant dimensions are certainly to be met with in such situations as the air vesicles of tubercular lungs, but on further examination such masses will be found to be in most cases mere clusters of cells surrounded by precipitated mucus or colloid. The author has never seen true giant cells arise by this method of fusion. They may frequently be noticed dividing, and the appearance may then be mistaken for one of conglomeration.

The author's own impression is that they are simply the enlarged offspring of some mesoblastic element, such as an endothelium or con-

nective tissue corpuscle. They are constant accompaniments of tubercular and syphilitic granulations, and, for some unexplained reason, where a porous foreign body is introduced into a tissue, they tend to accumulate in its spaces.

Iodoform and Giant Cells.—Marchand (No. 13, xciii.) has made the discovery that the application of iodoform to a wound, in a very short time destroys the giant cells; and explains its beneficial effect on tubercular sinuses, etc., upon this basis. They all disappear in a few days after its application.

201. **Fate of the Sponge—Absorption of Organic Textures.**—In course of time, the sponge becomes completely incorporated with the tissue. On examining parts in which a piece of sponge had thus become ingrafted, some months afterwards, the author was unable to discover any remains of it. It appears to become **dissolved** within the tissues, and entirely disappears.

The agency by which organic textures become absorbed when embedded in a tissue, has for a good many years been the subject of observation.

Metschnikoff's researches (*loc. cit.*, Sect. 189) have already been referred to, showing that the absorption of the tail in the frog's larva is effected by cells devouring the dead tissues, or, at any rate, invaginating pieces of dead tissue into their substance when these have become disintegrated.

It has long been supposed that dead bone is absorbed by the action of giant cells, or osteoclasts as they are called (Kölliker, No. 125, Wegner, No. 13, lvi., and Ziegler, No. 13, lxxiii.) Ziegler, however, has very properly pointed out that similar absorption goes on when such giant cells are not present. Lister supposed that catgut becomes disintegrated by cells of different kinds which invade it shortly after it is embedded in a wound. In some of the author's sponge experiments, it seemed that a slight excavation of the keratode could occasionally be made out opposite the point where a giant cell had become affixed.

Quite apart, however, from the fact that living protoplasm may take up tissue débris, the **liquids of the tissues** appear to have a peculiar **solvent** or **digestive** action. Mayer (No. 50, Aug. 17, 1878) found that many purely chemical substances brought about the disintegration of catgut when retained at a body temperature. Thus catgut No. 0 when placed in lime water became converted into a granular mass in twenty-two days. In blood serum a like result followed but required a longer time. Bile dissolved the albumins, but affected the gelatine-yielding constituents little. In urine the threads soon fell into a state of disintegration from solution of the cement substance.

The author has found that if catgut is run through the tissues of a **dead** animal kept at a body temperature, it undergoes disintegration in about the same time as is required in the **living**.

It is probable, that the juices of the tissue soften such textures and dissolve certain parts of them. There is, however, nothing against the view that leucocytes or other amœboid cells may remove the

débris or, at any rate, part of it, if they are abundant enough in the neighbourhood.

Sponge evidently becomes absorbed in very much the same way as catgut, only it requires longer time.

202. **Method of applying the Sponge.**—From the fact that new tissue can be built up so easily within the sponge, it might well be supposed that it would exert a most beneficial influence in causing **indolent ulcers** to heal. One of the chief causes of an indolent ulcer's not healing is the absence of the proper layer of young cicatricial substance upon its floor. A thin layer of **sponge** laid over the floor supplies the framework in which such may be formed in the same way as a **blood clot** does.

A great deal, of course, depends on how it is applied. The wound should first of all be rendered aseptic, and any sloughy shreds should be got rid of. A close-meshed Turkey sponge is the best for the purpose. It should be cut into thin sections in the freezing microtome and the larger they are the better. The sponge should be wrung out of freezing fluid "A" (Sect. 37), and be stuck on the freezer with mucilage. The sections should not be more than from $\frac{1}{16}$ to $\frac{1}{32}$ of an inch in thickness, and may be applied in one large continuous piece, or in several small ones. Great care should be taken that the sponge does not come nearer than $\frac{1}{8}$ to $\frac{1}{4}$ of an inch from the epithelial edge, as the latter will be sure to undermine it and prevent its adhering. In a few days it will be found to be filled with organising vascular tissue. A **second** layer, considerably smaller than the first, should now be placed on the surface, followed by a **third** and so on until the wound is healed. Indolent ulcers take on a remarkably healing and healthy look within a very short time of its application. The sponge before being cut must be soaked in dilute solution of caustic potash for several hours, and subsequently, in dilute nitric acid for a night. It should be thoroughly washed in water after this, and the sections may be kept in watery solution of carbolic acid (1 to 40) until required. With a large freezer (Fig. 14) great numbers of them can be thrown off in a few minutes, of exquisite delicacy and beautifully adapted to fit the irregularities of a wound. The dressing should be strictly antiseptic, the ordinary dextrine silk forming an excellent protective covering.

Although as yet the author has not had an opportunity of testing them, it has always seemed to him that the **calcareous** or **siliceous** sponges, such as those found in the Amazon, in which the skeleton is solid, would be most useful for the repair of bone. They are finely porous, can be readily shaped to any cavity, and hence should be well adapted for the organisation of bone where a more durable framework than that found in the ordinary **keratode** sponge is desirable.[1]

Literature on Sponge-Grafting. — **Acland:** Brit. Med. Journ., 1883, i. p. 205. **Atkinson:** Whitney Mem. Prize Essay, N. Y., 1885. **Booth:** Week. Med. Rev.,

[1] For an account of the recent applications to which sponge has been adapted in the healing of wounds consult Burnett, No. 147, i. No. 6, June 1885.

Chicago, x. 1884, p. 8. **Borck:** Week. Med. Rev., Chicago, viii. 1883, p. 351. **Burnett:** Med. Rec. N. Y., xxii. 1882, p. 500; *also*, Ann. Surg., St. Louis, i. 1885, p. 550. **Cody:** Trans. Med. and Phys. Soc., Bombay, ii. 1883, p. 39. **Franks and Abraham:** Journ. Anat. and Physiol., xvii. 1882-3, p. 349. **Hall:** Edin. Med. Journ., xxix. 1883-84, p. 806. **Hamilton:** Edin. Med. Journ., xxvii. 1881, i. p. 385; *also*, Brit. Med. Journ., 1883, i. p. 7. **Kendall:** N. Car. Med. Journ., Wilmington, xii. 1883, p. 144. **De Lautour:** Austr. Med. Journ., 1883, p. 145. **Matthews:** Week. Med. Rev., Chicago, vii. 1883, p. 438. **Perkins:** Brit. Med. Journ., 1883, i. p. 51. **Pokrovski:** Russ. Med. Voskresensk, i. 1885, pp. 294, 315, 330. **Sanctuary:** Brit. Med. Journ., 1882, ii. p. 1202. **Saylor:** Proc. Oregon Med. Soc., Portland, x. 1883, p. 144. **Thomas:** Pittsburg Med. Journ., iii. 1883, p. 129. **Thompson:** Med. Rec. N. Y., xxiii. 1883, p. 567. **Whitman:** Med. Rec. N. Y., xxii. 1882, p. 402.

203. **Cause of the organisation of Porous Bodies.**—Other hollow substances evidently organise after the same fashion quite irrespective of the material of which they are composed. There is, therefore, no specific property in the sponge. It is simply well fitted for the purpose on account of its porosity.

In attempting to explain why it is that such porous bodies become organised, considerable difficulty is experienced. The prime factor in the whole process seems to be the tendency which the blood pressure has to drive the superficial capillaries outwards when these are insufficiently restrained, and when surrounding conditions, such as those afforded by the sponge framework, favour their support. The other tissue changes seem to be secondary to this.

ORGANISATION OF BLOOD CLOT.

204. When blood is effused and coagulates upon an abraded surface it will, in course of time, become vascular, as originally pointed out by John Hunter, and more fully demonstrated by Sir J. Lister; and apparently becomes converted into cicatricial tissue.

Hunter (No. 128, iii. p. 244) showed that if blood is effused upon an exposed hollowed out wound, it may remain as a mere extraneous body, without itself acting upon the surface, but protecting the latter from external stimulation. The edges of the epithelium tend to contract over it as if it were a living tissue. The usual practice, he wrote, had been to scoop out this blood, and to apply warm dressings so as to encourage granulation. If it be left alone, however, the wound contracts and heals rapidly. He believed the **blood clot** to be a **living tissue** (p. 253), and described how blood effused into a tissue becomes vascularised (p. 243). Lister (No. 59, Nov. 19, 26, 1881, pp. 863, 901), has shown that blood effused into a wound acts as a protection against the invasion of putrefaction. He explains it by supposing that the living elements which cause its organisation confer upon it this property, and also that blood serum is not so favourable a soil for the growth of the organisms of putrefaction as is generally supposed.

The **blood**, after being effused from a blood-vessel, however, merely acts as a passive agent in bringing about organisation—it serves the same purpose as the *sponge framework*. Any vitality which its leucocytes may have exhibited immediately after effusion, is in a short time lost. In the mere act of coagulating a great many of the leucocytes

are destroyed (Schmidt), and remnants of these are always found in any fresh clot. Hence in a blood clot there are always relatively fewer colourless blood corpuscles than in an equivalent quantity of blood before coagulation.

The first thing that happens when blood is effused on a granulating surface or into a tissue is **coagulation**; at least, such is the first thing seen, when organisation is going to occur. Blood, which remains fluid when effused into a tissue, is either all immediately absorbed or becomes incapsuled by a layer of fibrous tissue. A mass of blood having coagulated in or upon a recent wound, the next thing observed is that the **blood-vessels** of the underlying parts begin to **dilate** and to become tortuous. The **connective tissue corpuscles** around them also commence to show unusual signs of activity. The interfibrillar spaces become œdematous, and each connective tissue corpuscle divides into several new cells, the young brood so produced occupying the spaces.

The next change perceived in the now tortuous and distended **blood-vessels** is that they are **displaced** and pushed outwards towards the clot which is lying on the surface of the wound. The blood clot is an excessively porous substance. It is more minutely porous than the finest sponge. The fibrin forms a network containing only a few blood corpuscles, while the serum is squeezed out of, or drains away from the interstices. It is, therefore, a tissue which, if its assumed vital properties be laid aside, is like a sponge in its structure, both being composed of a delicate framework with large and small meshes.

The blood-vessels which have been pushed into the clot from neighbouring parts bear with them great numbers of the actively proliferating connective tissue corpuscles, derived in the above-described manner from the adjacent connective tissues. Coming in contact with the blood clot, these penetrate into its interstices, and very soon fill its interfibrinous spaces. Almost immediately after this has taken place, the fibrinous network disappears—it falls to pieces—and the blood corpuscles of both kinds can be seen, at the edge of the clot, to undergo a similar fate. They become granular, colourless, apparently in some cases fatty, and then they disintegrate.

The **vascular loops**, surrounded by their tissue-forming cells, continue to penetrate further and further into the clot; and as successive meshes of the fibrinous network are filled by them, they cause its destruction, until the whole clot becomes in this way removed, *its place being taken* by new vessels and the above-described cicatricial elements. The latter soon elongate into spindle cells, and these, in from three weeks to a month, become transformed into fibrous tissue. (See further, Thrombosis, Sect. 206.)

ORGANISATION OF FIBRINOUS LYMPH—ADHESIONS.

205. *Fibrinous lymph*, or as it is sometimes called, a *false membrane*, is simply a modified **blood clot**. It is composed of the fibrin which

has been precipitated in the form of a network from the liquid part of the effusion accompanying an acute inflammation, in whose meshes is a greater or less number of leucocytes with sometimes coloured blood corpuscles. It is a blood clot with a disproportionate mixture of the elements; for while the *fibrin* and *leucocytes* are in great

FIG. 103.—ACUTE FIBRINOUS PERICARDITIS, ORGANISING (× 40 DIAMS.)

The section was made through the pericardium, the fibrinous effusion into the sac, and the myocardium. (*P*, *C*), pericardium, highly cellular; (*P*, *O*, *L*), pericardial organising layer of fibroblasts; (*F*, *E*, *S*), fibrinous exudation in the sac; (*M*, *O*, *L*), myocardial organising layer of fibroblasts; (*M*, *C*), myocardium (Picro-carmine and Farrants' Solution).

abundance, the *coloured blood corpuscles* are comparatively few. In certain instances even the leucocytes are so few in number that the false membrane appears to consist almost entirely of a dense mass of fibrin. False membranes, consequently, are extremely porous;

they have usually quite a sponge like consistence
79).

If a false membrane form in a **serous cavity**, su
cardium, the immediate effect is to cause the surfaces to a
there be not too great a quantity of serum present t
The union is slight and easily separable at first, but
weeks to a month becomes much firmer, owing to the fi
having been replaced by fibrous tissue; that which
fibrinous and temporary has now become fibrous and pe

The means by which this result is achieved in *all* se
alike. Let us take the **pericardium** in acute fibr
ditis as the basis of the description (see Fig. 103).

The **fibrin** coagulates upon the surface of the epic
that of the serous layer of the pericardium in **villus-lik**
layers in course of time coalesce (*F.E.S*), and the net
by its intertwining, forms the **temporary bond of u**
after this has occurred, the **vessels** in the pericardium
the epicardium and subepicardial tissue, become much d
tortuous, and, just as in the organisation of sponge or
thrown out from the surface into the meshes formed b
lymph. Contemporaneously with this, the whole of th
constituting the pericardium, the epicardium, and the
immediately underneath are thrown into a state of germi
and a host of **new cells** is thus formed. The **musc**
the wall of the heart sometimes even participate
elastic fibres which lie in the epicardium show no
of a progressive or retrogressive character. They ca
discovered forming a dark line in sections through
cicatrised pericardial adhesion.

A few **leucocytes** also exude after the acute inflam
and these mix with the cells derived from other sources.
vanish, however, very soon by a process of disinte
leucocytes which have been entangled primarily in the fi
become destroyed at a very early period, many probabl
coagulation. Those which are left become very gran
and fall to pieces. They lose their power of stainin
staining reagents, and hence are readily distinguish
fibroblasts which stain deeply.

As soon as the new **fibroblasts** are called into exi
pushed out on to the free surface, that is to say, into
sac. A **layer** (*M.O.L* and *P.O.L*), forms on each s
attached respectively to the surface of the heart (*M.C*),
cardium (*P.C*). This layer is composed of round an
and is identical in appearance with that which lies de
lating wound (Fig. 96 *f.*), or which is the means of unio
wound by the first intention.

As its cells are pushed farther and farther into th

they displace the fibrinous lymph and infiltrate its meshes. Long rows of such cells can be seen penetrating the fibrinous interspaces. Immediately on these becoming invaded, the network of fibrin falls to pieces and is absorbed, and as this absorption goes on from each side of the cavity, the amount of fibrin is steadily reduced in quantity and becomes more and more confined to the centre of the sac. The two **organising layers** ultimately *meet* and *coalesce*, at first partially with islands of fibrinous lymph between them, but afterwards without any intermediation.[1]

The round cells and spindles of which the two organising layers primarily consist become converted in time into fibres, so that before long a permanent **fibrous union** results.

If the steps of the process just described be compared with those of healing by the *first intention*, it will be noticed that in the two they are identical. In both, a layer of fibroblasts grows up respectively from each side of the wound or serous cavity. In both, the lymph or blood clot which temporarily retains the surfaces in apposition is absorbed; and in both the source of the permanent adhesion is to be sought in *a growth* of the new cellular elements from the old.

Literature on Organisation of Porous Substances, Blood-Clots, etc.—**Ball**: Dub. Journ. Med. Sc., lxxiv. 1882, p. 280. **Foulis**: Behaviour of B.-Clot under Antiseptic Conditions, 1877. **Lamallerée** (Animal Graft): Soc. de sc. méd. de Ganat, Compt. rend., xxxv. 1881, p. 42. **Porritt**: Edin. Med. Journ., xxvii. 1881-2, p. 975. **Rosenberger**: Arch. f. klin. Chir., xxv. 1880, p. 771. **White**: Med. Rec., N. Y., xxiii. 1883, p. 564. **Ziegler** (Giant-cells and Leucocytes): Centralbl. f. d. med. Wissensch., xii. 1874, p. 801.

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[1] Whether the blood-vessels inosculate from either side the author cannot say; Virchow was able to inject the one side of certain adhesions from the other.

CHAPTER XIX

HEALING OF WOUNDS AND ORGANISATION—(*Continued*)

THROMBOSIS AND HEALING OF BLOOD-VESSELS.

206. **Definition.**—*By a thrombus is meant a clot locally formed within the heart or a blood-vessel.* In the case of a vein it is known as a venous thrombus in that of an artery as an arterial.

207. **Determination of Coagulation.**—The conditions which cause the blood to coagulate within a vessel are probably as yet not thoroughly understood. Richardson's (No. 220, 1858, p. 193 and *seq.*) and Brücke's (No. 13, xii. and No. 148, January 1857, p. 183) researches have shown that the mere **interruption** to the flow of blood through the channel of the vessel is not sufficient to occasion it; and Lister's experiments (No. 59, 8th Aug. 1863) have added much confirmatory evidence to these results. When a vessel is **doubly ligatured**, it by no means necessarily follows that the blood within it coagulates.

By all the early workers on this subject, such as Virchow (No. 129, pp. 219-732), Cohnheim (No. 31, i. p. 134), Zahn (No. 13, lxii. p. 81), Baumgarten (No. 50, 1876, No. xxxiv.), and Hlava (No. 104, xvii. 1883), it has been taken for granted that the colourless corpuscles are in the closest manner related to thrombus formation. Zahn (*loc. cit.*), from observations on the living mesentery of the frog, found that when the wall of a vessel was injured, the colourless corpuscles accumulate round the injured part, constructing what he called a **white thrombus.** The corpuscles subsequently, in great part, disintegrate and give rise to a granular accumulation which, by its action upon the fibrinogen of the blood, causes a precipitation of fibrin. Red corpuscles are afterwards liable to become entangled in the mass, and thus an ordinary **red thrombus** may result. Wooldridge's experiments (No. 149, 1881) had a like tendency, in attributing the coagulative powers of the blood to the leucocytes contained in it.

The discovery of the **hæmatoblasts** or **blood plates** in the blood by Hayem and Bizzozero (see Sect. 145) has given a new impetus to the study, with the effect, that of late years some very important additions have been made to our former knowledge. These hæmato-

blasts have a peculiar tendency to adhere to any foreign bodies, and are destroyed in the act of coagulation.

208. **Eberth and Schimmelbusch on Thrombosis.**—Eberth and Schimmelbusch (No. 13, ciii. 1886) have studied the early stages of thrombus formation in the living mesenteric vessels of warm-blooded animals (guinea-pig and dog) with great care, and the summary of their results is briefly, as follows:—When the mesentery is first exposed, with due precautions (see Sect. 165), the circulation shows, as in a cold-blooded animal, an **axial** and a **peripheral stream.**

The blood plates run with the coloured blood corpuscles in the axis while the colourless corpuscles roll along in the periphery, a few of them getting occasionally tossed into the axial current.

As the current becomes slower, the leucocytes tend to be retarded in their progress onwards, and accumulate in the periphery. In course of time, the blood plates also separate from the blood current and similarly accumulate at the periphery. When a vessel is injured, as by tying a ligature round it and removing this in a quarter of an hour afterwards, the blood plates have a peculiar tendency to *adhere* to the injured part of the tunica intima (see same authors, No. 13, cv. p. 331), and to each other.

This mere **conglutination,** as they call it (No. 13, cv. p. 456), is different from the act of **coagulation**, which in reality is a process of crystallisation.

A **thrombus-like mass** of blood plates is thus constituted, and it is this which serves as the basis of the future thrombus.

The authors find, however, that it is not every injury of the wall which will bring this about. It is specially where **irregularities** of the tunica intima are present, that such a thrombus is deposited. So long as the circulation within the vessel is natural, the blood plates, floating as they do in the axial current, never touch the wall, and if the stream is not interrupted in its course, the mere injury to the wall will not occasion it. It is, therefore, the **impingement** of the blood plates against the irregularities of the wall which they regard as the essential factor, and hence the readiness with which thrombotic deposits take place on cardiac vegetations and on the wall of a vein roughened by phlebitis. These blood plates, as the circulation through the obstructed vessel becomes impeded, determine the formation of fibrin, and this entangles more and more of the coloured corpuscles in its meshes.

Bizzozero's Observations.—Bizzozero's results (No. 13, xc. p. 261) entirely coincide with these. He states that, if a vessel of the mesentery is simply *pinched*, the *blood plates* accumulate round the injured wall in abundance, and further, that pieces of these may become detached and carried off in the current as **blood-plate emboli.**

209. **Hayem's Results.**—Hayem's experiments on thrombosis (No. 40, xcvi. No. x.) point in the same direction. He has also studied the effect of the introduction of certain substances into the circulation upon the power possessed by the blood of precipitating a thrombus (No.

40, xcvii. No. iii.). He doubly ligatures the jugular vein on the one side, injects the substance to be experimented with into the circulation, and afterwards ligatures a corresponding part of the jugular vein on the opposite side. The blood in the former remains fluid for a long time, but that in the latter coagulates with a rapidity corresponding to the substance injected. One of the most powerful means of determining **coagulation** is the injection of the animal's own **serum**, or that of an animal of the same genus. Distilled water, solution of fibrin ferment, 0·6 per cent solution of common salt, and blood defibrinated or not, raise the coagulability. Serum taken from another animal, as for instance, ox serum injected into the dog, occasioned a form of **curdling** but not true coagulation.

Literature on Coagulation of the Blood.—**Allara**: Gazz. med. ital. lomb. Milano, iii. 1881, p. 105. **Bojanus**: Beiträge z. Physiol. u. Path. d. Blutes, 1881. **Cadet**: Étude physiol. d. éleménts figurés d. sang et en particulier des hæmatoblasts, 1881. **Duane**: N. Y. Med. Journ., xxxiv. 1881, p. 1 *et seq.*; *Ibid.*, xxxv. 1882, p. 343. **Fano**: Centralbl. f. d. med. Wissensch., xx. 1882, p. 210. **Feiertag**: Beobachtungen üb. d. sogennanten Blutplättchen, 1883. **Frédéricq**: Rev. scient., xix. 1880, p. 537. **Freund**: Wien. med. Bl., ix. 1886, p. 296; *also*, Med. Jahrb. Wien, i. 1886, p. 46. **Gamgee**: Notes on . . . non-existence of Ammonia in Blood, 1865; *also*, Some Old and New Experiments on the Fibrin-ferment, 1879; *also* (Excellent Historical Account), Physiological Chemistry. **Hammersten**: Archiv. f. d. gesamt. Physiol., xvii. 1878; *Ibid.*, xviii. 1878; *Ibid.*, xiv. 1877; *Ibid.*, xix. 1879. **Hasebroek**: Ztschr. f. Biol., xviii. 1882, p. 41. **Haycraft**: Birm. Med. Rev., xvii. 1885, p. 193; *also*, Journ. Anat. and Physiol., xxii. 1888, p. 172. **Henry**: Arch. Med., N. Y., xii. 1884, p. 242. **Hoffmann**: Beitrag zur Physiol. u. Path. d. farblosen Blutkörperchen, 1881. **Holzmann**: Arch. f. Physiol., 1885, p. 210. **Howell**: Johns Hopkins Univ. Circ., Balt., iii. 1884, p. 128; *also* (New Elements), Science, Camb., iii. 1884, p. 46. **Kemp**: Am. Month. Micr. Journ., vii. 1886, p. 181. **Laker**: Sitzungsh. d. k. Akad. d. Wissensch., lxxxvi. 1882, p. 173. **Lingbeek**: Over het klinisch onderzoek der morphologische bestanddeelen van het bloed, 1884. **Löwit**: Beiträge z. d. Lehre v. d. Blutgerinnung, 1884; *also*, Prag. med. Wochnschr., xi. 1886, p. 63. **Mayet**: Arch. de Physiol., ix. 1882, p. 1. **Norris**: Lancet, 1883, ii. p. 136 *et seq.* **Picot**: Gaz. heb. d. Sc. méd. de Bordeaux, iv. 1884, p. 28. **Renaut**: Arch. de Physiol., viii. 1881, p. 649. **Robin**: Journ. de l'Anat. et Physiol., xvii. 1881, p. 331. **Salvioli** (Diastatic Ferment): Centralbl. f. d. med. Wissensch., xxiii. 1885, p. 913. **Sappey**: Les éléments figurés du sang, etc. 1881. **Schmidt**: Haematologische Studien, 1865; Archiv. f. d. gesamt. Physiol., xi. 1875; Archiv. f. Anat. u. Physiol., 1862; Ueber Menschenblut u. Froschblut, 1881; Arch. d. Phys., ix. 1882, p. 513; *Ibid.*, xi. 1883, p. 112. **Weigert** (Review of Latest Theories): Fortschr. d. Med., i. 1883, pp. 373, 405. **Wooldridge**: Journ. Physiol., Camb., iv. 1883, p. 367; *also*, Practitioner, xxxvi. 1886, p. 187.

ORGANISATION OF THE THROMBUS.

210. When a vessel becomes occluded by a thrombus, there is a great tendency for the latter to become **organised**. The organisation commences nearest the wall (see Fig. 104) and spreads inwards. A layer of round and spindle cells forms at the periphery of the thrombus and gradually encroaches upon it. Blood-vessels are abundantly projected into the clot along with these organising elements, so that a species of **granulation tissue** (*g,g*) comes in course of time to occupy the lumen of the vessel.

While the thrombus is young its channels can be readily filled with

injection from the main trunk, and this, as pointed out by Paget (No. 23, p. 208), was taken by John Hunter and Stilling to signify that the clot became vascular from the channel of the occluded vessel independently of the vessel wall. According to Paget the **vessels** usually enter the organising clot in dogs in the **fourth week,** by which time it has become partially organised. The author's own observations on vessels ligatured after amputation in the human subject coincide with this. They are usually found about the end of the third week in considerable abundance.

FIG. 104.—ORGANISING THROMBUS. INTERNAL SAPHENOUS VEIN (×50 DIAMS.)

(*a*), Laminæ of thrombus; (*b*), tunica intima from which processes (*g,g*) are projected into the thrombus; (*c*) muscularis; (*d*) areolar coat; (*e*) fat outside the same; (*f*) small artery (Picro-carmine and Farrants' Solution).

Weber's beautiful injections (No. 115, i. p. 144) of divided and ligatured arteries show that they are derived from the **vasa vasorum.** Any other channels which can be injected from the continuity of the vessel above, are merely **fissures** in the clot. The blood-vessels generally sprout out from the lacerated tissues close by the ligature. He figures a distinct continuity of the above channels with the latter, but such appearances are deceptive. The vessels

seem to sprout from the lacerated coats of the vessel like granulation loops.

As they are pushed inwards, they carry with them **organising elements**, and these ramifying throughout the thrombus, cause its destruction, and ultimately its absorption. They, however, furnish the materials for organisation, and it is by means of **these**, not out of the **clot**, that the permanent cicatrisation is effected.

Partial Organisation.—Sometimes a vessel may be seen in which the cicatrisation is only partially effected, from portions of the thrombus having been **absorbed** or **tunnelled** out before being infiltrated with the new elements. By the meeting in the centre of the lumen of the organising masses of granulation-like tissue, and by their coalescence, several channels may thus be established through which blood ultimately circulates. This, however, is unusual. Where the thrombus is extensive, it most commonly happens that, partly by the **uniform thickening** of the tunica intima caused by the deposition of cicatricial elements within its substance, partly by the projection inwards of granulation loops, the whole channel becomes completely obliterated. A little pigment is all that remains of the original thrombus.

Origin of New Elements.—While, as just remarked, there is not much doubt that the thrombus organises from its periphery to its centre, there is very considerable diversity of opinion as to where the new elements come from.

Baumgarten (No. 50, Aug. 19, 1876, No. xxxiv.), describing the process as occurring in a doubly ligatured artery in the rabbit, traced them to the **tunica intima**, and more particularly to its endothelium. The new elements he said accumulate in the folds of the inner elastic lamina, and gradually encroach upon the thrombus, which meanwhile softens in the centre. From the points of ligature above and below, new tissue is also projected inwards. The part taken by the **clot** in organisation is absolutely *nil*. Waldeyer's (No. 13, xl. pp. 379 and 391) and Thiersch's (No. 115, i. pp. 550, 556) researches practically point to the same issue.

In the year 1879, however, Senftleben, working under Cohnheim's direction, published a paper (No. 13, lxxvii. p. 421) in which he endeavoured to disprove what Baumgarten and others had recorded of the source of the new elements, with a tendency to revert to the old idea of the organisation from leucocytes. His conclusions mainly rested on what is known as the **Senftleben experiment**, which consisted in doubly tying a vessel such as the **aorta** in an animal (rabbit) which had been dead for three days, and introducing it into the abdomen of a second. He found that the piece of vessel becomes organised in exactly the same way as one which is living, and in course of time is obliterated by granulation tissue provided with abundant blood-vessels forcing its way into it. He concluded that the endothelium here could have nothing to do with the process.

Schultz (No. 130, ix. p. 84; No. 50, Mar. 2, 1878, No. ix.) supported these views. He could perceive no proliferation of the endothelium in a doubly ligatured living vessel; and by using coloured particles such as **cinnabar**, he made out that the cells outside the vessel absorbed them and afterwards found their way through its wall into the thrombus. He takes for granted that they were **leucocytes**. The same thing occurs when an artery is closed by a single ligature.

Burdach (No. 131, and No. 13, c. p. 217, 1885) has repeated Senftleben's experiment with the **carotid artery** of dead oxen and rabbits, and found that, as Senftleben had affirmed, the interior of the vessel becomes filled with organising tissue containing numerous blood-vessels and cells. These, however, he declares got in, not through the intact wall of the vessel, but from its injured ends. Raab (No. 132, xxiii. p. 156; and No. 50, May 31, 1879) looks upon the endothelium as the exclusive source of the elements of repair; while Foa (No. 133, iii. No. iv.) and Pfitzer (No. 13, lxxvii. p. 397) trace them to both the endothelium and to the penetration of granulation tissue through the wall.

The **author's own observations** lead him to believe that the whole of the tissues of the tunica intima, endothelium included, are the means of initiating the organisation; but that vessels, in course of time are projected into the thrombus from the wounded or from the sound parts of the wall, which aid in completing the process by furnishing new fibroblasts which ramify throughout the clot.

The Senftleben experiment proves nothing. We have seen (Chap. xviii.) that any hollow body introduced into the peritoneal cavity becomes organised. No doubt, the wall of the dead vessel he employed, like any other animal tissue, became softened and pervious within a few days after its introduction, thus allowing organising vessels and cells to penetrate it readily. That these cells were **leucocytes** he fails entirely to verify; so that this experiment certainly does not disprove that the living **tunica intima** may participate in the process. It simply adds one more fact to what was already known, namely, that a ligatured hollow animal tube will become filled with organising tissue if placed under proper circumstances.

Literature on Thrombosis.—**Baumgarten:** Berl. klin. Wochnschr., xxiii. 1886, p. 385. **Bizzozero:** Centralbl. f. d. med. Wissensch., xx. 1882, pp. 17, 563. **Buettner:** Ueb. Thrombose u. Embolie, Berl., 1874. **Delépine:** Brit. Med. Journ., 1887, ii. p. 408. **von Düring:** Deut. Zeitschr. f. Chir., xxii. 1885, p. 425. **Eberth and Schimmelbusch:** Fortschr. d. Med., iv. 1886, pp. 115, 417, 581. **Freund:** Med. Jahrb., Wien, i. 1886, p. 46. **Hanau:** Fortschr. d. Med., iv. 1886, p. 385. **Hayem:** France méd., i. 1883, p. 366. **Humphry:** Coag. of Blood in Veins, Camb., 1859. **Nonne:** Deut. Arch. f. klin. Med., xxxvii. 1885, p. 241. **v. Recklinghausen:** Arch. f. path. Anat., C. 1885, p. 503.

CLOSURE OF A LIGATURED ARTERY.

211. The appearances, as regards the thrombus at least, in ligatured arteries, vary greatly, according to whether the vessel be secured with **catgut**, under antiseptic precautions, or whether it be ligatured with **silk**, and putrefy. In the former case, the clot which is found in the ligatured vessel is extremely small and filiform, seldom filling the vessel, and is sometimes practically absent; while in the latter, it usually is voluminous and extends up to the first branch of any size. The vessel nevertheless closes as quickly, if not more so, in the former than in the latter, and the process ends by the vessel becoming converted into a fibrous cord *in whatever portion the blood has ceased to flow.*

The closure of the channel undoubtedly takes place in the manner previously described (Sect. 210), namely, by a **thickening** of the **tunica intima**, more especially in parts distant from the ligature, and by **granulation tissue** being forced into the vessel at the point of occlusion. The formation of a thrombus within it is quite unnecessary.

When a ligature is applied in the **continuity** of an artery or to a **divided artery** in a wound, provided the ligature be at some distance above the cut end, the obliterative process seems to go on both above and below. The part below the ligature becomes infiltrated with granulation tissue, and if it dies, is in course of time absorbed.

It is seldom that the thickening of the tunica intima is symmetrical when the vessel is ligatured (Fig. 105).

Fig. 105.—Cross Section of an Artery a short distance above the ligature (×50 Diams.)

(*a*) Tunica adventitia; (*b*) thickened tunica intima; (*c*) inner elastic lamina (Picro-carmine and Farrants' Solution).

Fate of the Ligature.—In the case of **catgut**, little, if any, trace of the ligature will be found after **thirty days**. Round large trunks at the point of deligation, there is in Man after this time a narrow **fibrous ring** similar to that recorded by Lister in the calf (No. 59, Feb. 5 and 12, 1881, pp. 201, 275). The dead tissue, as he remarked, becomes superseded by the living. **Silk** remains longer in the tissue, and the result justifies such an assertion even more than in the case of catgut. It acts primarily as the *mould* in which the *natural ligature*—composed of living cicatricial tissue—becomes shaped; but being an animal structure, it is itself in course of time absorbed.

212. **Healing of an Artery when simply Wounded.**—If an artery be wounded, and if a ligature be not applied, it may heal spontaneously, although there is great danger of hæmorrhage coming on even when organisation has pretty well advanced. The blood

coagulates round the cut edges of the wall by the **blood plates** accumulating upon it (Sophie Lubnitzky, No. 104, xvii. 1883). There sometimes forms round the wound a sac-like or **aneurismal mass** (Zahn and Pfitzer). The edges of the wound never unite by **primary** union. Into the wound or rather the clot obstructing it, there then grows a quantity of **granulation tissue** from without, the vessels of which bear with them the elements of repair, and in this way it is closed.

213. **Closure of Vessels from other Causes.**—The vessels of the **embryo**, which in extra-uterine existence cease to transmit the blood, are closed by a thickening of the tunica intima, similar to that just described, and the same may be said of those of the **uterus** after utero-gestation. In various **pathological states** the arteries become narrowed or occluded, also by a thickening of the tunica intima (see "arteriitis obliterans"); and in all these cases it occurs irrespective of the deposition of a thrombus. In fact, as Paget (No. 23, p. 207) remarks, *when any part of an artery, through any cause, ceases to be traversed by blood* its lumen becomes obliterated. The means by which this is accomplished is by a deposition within the intima of new cicatricial materials. These give rise to a thickening of the intima, which, encroaching more and more upon the channel of the vessel, in course of time obliterates it.

Literature on Healing of Blood-vessels.—**Guthrie**: Diseases and Injuries of Arteries, 1830. **Hodgson**: Diseases and Injuries of Arteries, 1815. **Lee**: Lectures on Subjects Connected with Practical Path. and Surg., i. 1870. **Liddell**: Intern. Encycl. of Surg., iii. 1883. **Moore**: Holmes' Syst. Surg., i. 1870, p. 712. **Shakespeare**: Lectures on Repair in Arteries, 1879. **Tillmans**: Berl. klin. Wochnschr., xviii. 1881, pp. 33, 35; *also*, Internat. Journ. Med. and Surg., N. Y., i. 1881, p. 223. **Treves**: Brit. Med. Journ., 1881, i. p. 232. **Warren**: Healing of Arteries after Ligature, 1886.

REGENERATION OF SPECIAL TISSUES.

214. **Epithelium.**—Each tissue *in the adult* reproduces its like. The process, in fact, is one of true **growth** not of **development** (see Sect. 119). In no tissue is this more strikingly exemplified than in epithelium. There is absolutely no evidence to show that epidermis or any other epithelium ever springs from anything unless a pre-existing tissue of a like kind. The old cells divide, and from the resulting progeny the new epithelium is generated. The process of division usually seems to be indirect (see previous references Section 193).

Wolfe (No. 193, Jan. 1884, and No. 194) has succeeded in transplanting the whole of the tissues of the **conjunctiva** of the rabbit on to that of Man in order to fill a gap caused by cicatricial contraction.

Skin grafting (see Sect. 193).

215. **Fibrous Tissue.**—Sufficient has been said of the manner in which this is reproduced, when describing the process of cicatrisation,

to show that, like epidermis, the new is the direct offspring of the old. It only remains to notice what occurs in the union of **divided tendon**.

Experimenting on rabbits, Paget and Savory (No. 23) found, that at the instant of division of the Achilles tendon the divided ends separate to a distance of nearly an inch, the upper portion of the tendon being drawn up the leg by the action of the gastrocnemius and soleus muscles. The retraction is greater than in operations on the human Achilles tendon. The separation is effected entirely by the withdrawal of the upper end of the tendon, the lower end, having no muscular attachment, remains opposite the wound.

It seems probable that the next stage consists in the effusion of a more or less highly **albuminous liquid** into the sheath. Sometimes a little **blood** (Feltz, No. 49, 1868) is effused as well, and from the end of the third or fourth day this exudate becomes permeated with spindle-celled **fibroblasts** derived neither from the blood leucocytes nor from the cells of the primarily effused plasma.

Bizzozero (No. 134, vol. cxl. No. xl. 1868) states that few of these arise from the *sheath* of the tendon, but rather from the *loose connective tissue* enveloping the divided end of the tendon. Dembowsky (No. 135) and Güterbock (No. 13, lvi.), on the other, hand have traced the new cells to a proliferation of those already existing in the sheath of the tendon, while the tendon itself remains quite passive.

From the fact that the connective tissue nuclei of tendon, when stimulated, readily proliferate (Ranvier, Güterbock, Spina, Feltz, and Ginsburg), it seems probable that the divided ends are capable of throwing out, in certain cases at least, new cell elements which may serve for reparation purposes, just as divided fibrous tissue does in an ordinary wound. This, however, would not necessarily preclude the sheath from subserving a similar end. The actual process of organisation of these cells is similar to that in other parts.

216. **Muscle.**—Striated muscle seems, as before remarked, to reproduce itself with difficulty. If a large wound, such as that resulting from an amputation of a limb, be examined in about a month after its infliction, the muscular fibres will be found to have in great part disappeared from their sheaths, wherever it happens that a portion of a muscle has become implicated in the cicatrix. The muscle swells, becomes homogeneous, and is afterwards absorbed, while the *endomysium* and *perimysium* become much thickened. It occasionally happens, however, that new striated muscle fibres grow out of the spindles of a young cicatrix. These have doubtless originally sprung from muscular tissue.

Helferich asserts that he found a piece of muscle from an animal, substituted for human muscle, unite with the latter.

217. **Bone.**—The regeneration of bone readily occurs in any part into which osteoblasts have found their way. The process is beauti-

fully illustrated in the growth of *osteophytes* from pieces of periosteum detached in a comminuted fracture, or in periostitis.

Ollier (No. 195, i. p. 413) succeeded in transplanting periosteum from one leg in the rabbit to the deep muscles of the opposite. MacEwen (No. 95, ii. 1882) utilises **fragments** of bone for the purpose of regenerating part of a bone that may have been lost. The grafts ought to be interhuman, and should comprise all the elements of the bone.

218. **Nerve**—*Recovery of Function.*—The regeneration of divided nerves has long occupied much attention, and is a matter of very great interest. That the **function** of a nerve may be regained, and that a more or less perfect **union** of the divided ends may occur after section cannot be doubted in view of the evidence derived both from cases in Man and from experiments on the lower animals. Several interesting problems are suggested thereby. In the first place, by what means is it that the union of the divided ends is brought about? In the second place, how is the union so effected that the fibres of the upper end seem to select those in the lower which functionally correspond with them? In the third place, do the peripheral branches retain their integrity, or do they die and become replaced by new nerve fibres pushed out from the old?

Paget (No. 23) found that in the case of a divided **median nerve** sensation began to return in the parts supplied by it within ten days to a fortnight, and by a month's time the nerve had almost completely recovered its function.

Still more remarkable facts, however, have been recorded by Gluck (No. 13, lxxii. p. 624) in experiments he made upon the **sciatic nerve** in **fowls.** He found that when a piece of a nerve 1 centimètre long is cut out, a cicatrix forms between the two ends which, even after three to four months, did not show any regenerated nerve fibres. When the nerve was simply divided, however, and the ends stitched together, a bond of union was rapidly established between them. Spindle cells developed within seventy-two hours which arranged themselves linearly. They were in connection with the sheath of the central and peripheral stumps of the nerve, and brought about the union of the same. Amyelinic nerve fibres appeared in eight days, round which a medullary sheath was gradually deposited. In the central end there was no degeneration of nerve fibres, while in the peripheral, there was only a minimum amount of it. After eighty hours, there was a complete organic coalescence of the separated ends by a soft glassy intermediate tissue, as yet poor in cells, but in which capillaries were to be seen.

After **excision** of a piece of nerve, **restoration of function** did not follow, but when it was simply **divided** and the ends carefully brought together, the restoration of function took place so rapidly that he found it to be perfect in two instances *within twenty-four hours.* He concludes that the **granulation tissue** must have been the means of conduction in these cases.

The usual issues of these experiments on the sciatic were that, when divided and the ends accurately adjusted by means of catgut sutures, the muscles supplied by the nerve remained totally paralysed for **fifty hours.** By the end of this time the animal had *partially* regained the use of the paralysed muscles. In **seventy-two hours** the recovery was very marked; and in **eighty-six hours** the limb readily replied reflexly to stimulation of the foot. To make perfectly certain that the impulses were propagated along the trunk of the nerve, it was laid bare above

the point of division; a glass plate was inserted underneath it; and it was stimulated electrically and mechanically over this, with the result, that the muscles supplied by the nerve readily contracted.

Vanlair's experiments (No. 136) seem to prove something further, namely, that the regenerated fibres have the same **topographical distribution** as before division. He first divided the sciatic, brought the ends together, and allowed the wound to heal and the nerve fibres to be regenerated. A main popliteal branch was now divided and it was seen that the muscles paralysed corresponded to the normal distribution of the nerve. Contrary to what Gluck and others hold, he found, as Waller had previously described (No. 137, July 1852), that the peripheral end degenerates and that the new nerve fibres are pushed into the sheath of the old from the proximal end. He consequently regards the complete recovery of function and its topographical distribution as all the more extraordinary. Ranvier has pointed out the preponderating influence of mechanical conditions, such as the opposition offered by the tissues, in the guidance of the distribution of regenerated nerves. Vanlair thinks that the old sheath being that in which there is least resistance, the new nerve fibres are naturally prolonged into it.

Paul Bert's experiments on the rat's tail seem to lend some support to the view that the new nerve fibres are simply *pushed out* from the old. Into a wound of the back of a rat he introduced the tip of the tail and allowed the two to become united. On subsequently cutting off the tail at the root and irritating the stump he found that the animal evidently experienced pain. There must, therefore, have either been some anastomosis between the nerves of the wound and those of the tail or the former must have been pushed into the tail tissues. We also know that **cicatrices** become sensitive and that nerve fibres can be traced into them.

Source of Materials of Repair.—There seems to be the greatest diversity of opinion, even at the present day, as to where the **new materials** for the bond of union come from, and as to what happens to the **peripheral portion** of the nerve. The literature on the subject has become so voluminous that it is impossible to do more than glance at the chief views that are held in regard to these points. The chief matters of dispute are whether the *peripheral part* of the nerve always *degenerates* or whether it becomes united continuously with the *proximal* by a new cicatrix-like tissue, and if so, where this cicatrix-like material comes from.

As before mentioned, Waller and Vanlair (*loc. cit.*) were of opinion that the regeneration went on entirely from the central end, and that the peripheral degenerated. Colasanti (No. 51, Part I. p. 206, 1878) found that the peripheral fibres degenerated as far down as the next Ranvier's ring. Both the medullary sheath and axis cylinder became fatty down to this point. Tizzoni (No. 50, No. xiii. 1878) describes the degeneration as affecting both divided ends, but the peripheral more than the proximal. It always commences at the Ranvier's rings, and spreads thence towards the middle of the interannular space. The myeline sheath and axis cylinders fall to pieces. Neumann (No. 14, xviii. p. 302) made out that the peripheral part of the nerve always degenerates, and that the regeneration is brought about from the central end and always spreads centrifugally.

On the other hand Schiff (No. 138, 1852, and elsewhere), Philippeaux and Vulpian (No. 40, xlviii. 1859, No. xv. and elsewhere), Hjelt (No. 13, xix. p. 352), Krause (No. 139, xx. p. 1), Magnien (No. 36, 1866, i. p. 115), and Erb (No. 140, v. p. 43, 1868) maintain that the axis cylinder at least is preserved in the peripheral part.

A good deal seems to depend upon whether the nerve is merely *divided* and *accurately adjusted*, or whether a piece is actually *cut out*. In the latter case, the peripheral part seems, so far as the author's own experiments on the sciatic nerve in toads indicate, to *suffer complete destruction* from coagulation of its myeline and subsequent fatty degeneration of the whole fibre unless the fibrous sheath, as Waller had previously demonstrated. When the ends are *accurately held together*, however, so as to ensure that union will take place by the first intention, a large number at least of the nerve fibres appear to *retain their integrity*.

Local Origin.—Where a reproduction of nerve fibres takes place **locally**, and where the axis cylinders of the proximal stump are not merely pushed into the sheath of the peripheral, Gunther and Schön formerly (No. 64, 1840) traced their regeneration to a plastic lymph which was effused between the cut ends.

In more recent times, however, two views have chiefly been taken of their genesis. The first of these is, that the new fibres are evolved out of **spindle cells** arranged end to end; and the second, that they are derived from the old nerve fibres by a **splitting of the axis cylinders** within the original sheath of Schwann, followed by a projection of the filaments into the wound.

Of the believers in the former theory, Lent (No. 100, vii.) and Bruch (*Idem.* vi.) suppose that the spindles are derived from the fibrous nerve sheath. Beneke (No. 13, lv.), on the other hand, traced the origin of the spindles to an endogenous proliferation of the nuclei of the sheath of Schwann, a medullary coating being deposited in course of time around them; while Hertz (No. 13, xlvi.) saw them arise from both sources. Neumann (No. 126, Jahrg. ix.; and No. 14, xviii. p. 302) derived the young nerve fibres from very much the same source as Beneke, namely, from an endogenous growth of nuclei within the Schwann's sheath. These are converted into delicate fibrils which, in course of time, may fill the sheath and become surrounded by a protoplasmic mantle, the future medulla.

Eichorst (No. 13, lix. p. 1) gives a more rational and accurate description of the process of regeneration under such circumstances. The nerve fibres of both ends, he says, participate in the organisation. The medullary sheath becomes destroyed, and it is from the **axis cylinders** that the new connecting nerve fibres are derived. This is brought about by their **splitting** into a number of fibrils both at the central and peripheral ends. This splitting takes place within the Schwann's sheath, so that the latter, in course of time, becomes distended with them. The central fibrils are then pushed outwards through the cicatrix to meet the peripheral, and a coalescence follows. He affirms that the nuclei of the Schwann's sheath proliferate, but denies that they have anything to do with the regeneration of nerve fibres.

Mayer (No. 141, 1881) describes virtually the same method.

TRANSPLANTATION OF FŒTAL TISSUES.

219. Zahn (No. 13, xcv. p. 369), in a communication to the International Medical Congress, brought forward some curious facts

bearing on the above. He formerly found that small pieces of **rib cartilage**, when taken from the **adult** and immediately transplanted into the tissues of another animal, underwent merely **retrogressive** metamorphosis. More lately he has discovered that when taken from the **embryo** and transplanted into various localities, the tissue continues to live and grow. **Cartilage**, **bone**, and ordinary **connective fibrous tissue** succeed best. He utterly failed to get the tissues of various kinds of tumour to grow, nor could he excite in any tissue the peculiar atypical conditions necessary to induce the growth of a tumour from it.

V. Kahlden and Schottelius (No. 196, 1881; and No. 104, xiv. p. 229) were similarly unsuccessful.

General Literature on Organisation.—**Dutrochet:** Structure intime des animaux et vegetaux, 1824. **Goodsir:** Memoirs, i. 1868. **Lohe:** Ueb. d. Antheil d. weissen Blutkörperchen b. Bildung d. norm. u. path. Gewebe, 1869. **Schede** (Blood-clot): Deut. med. Wochnschr., xii. 1886, p. 389. **Schwann,** with notes by Schleiden: Structure and Growth of Animals and Plants (transl.), Syd. Soc., 1847. **Travers:** Physiol. of Inflam. and the Healing Process, 1844.

CHAPTER XX

ULCERATION

The Different Forms of Ulcer.

220. **Definition of Term.**—*An ulcer is an open wound which, instead of healing, tends to remain stagnant or to progressively invade neighbouring parts.*

221. **The Indolent Ulcer.**—The typical site is on the lower extremities, notably between the calf and ankle. It is more usually present in a person in middle life than in youth or old age, and more frequently in males than females. It will generally be found to have been neglected, the patient having been walking about and improper dressings having been applied.

The edge is raised, hard, and frequently has a blanched callous aspect. Its border is occasionally somewhat irregular, and it appears to be deeply excavated, partly on account of the loss of substance, partly from the elevation of the infiltrated edge. The floor is either devoid of granulations or they occur in irregular patches, and are ill formed. It has a glistening, scooped out appearance, and from it is discharged a quantity of sanious thin liquid. There is little attempt at healing, and if it has been irritated from the patient's movements, the surrounding parts may display a red inflammatory blush.

The cause of the **indurated edge** is twofold, firstly, the undermining of the epidermis by *dilated vessels* and *half-organised granulation tissue.* Not unfrequently the vessels rupture and blood is effused in considerable quantity. Secondly, it is materially augmented by the *accumulation of the epidermis* in a dense mass, which pushes its way downwards into the underlying tissues in the form of long club-shaped or tuberose processes instead of spreading over the wound in a thin pellicle. One of the chief causes of the ulcer's not healing seems to be the distension of these vessels and the accumulation of unorganised granulation tissue underneath the epidermic edge. Pressure applied to the part acts beneficially in causing the wound to heal, apparently by restraining the vessels.

The floor of the wound exhibits few embryonic cicatrix-forming elements. It is usually constituted simply by the exposed fasciæ and sheaths of tendons, covered by a thin layer of abortive granulation tissue. The blood-vessels upon it are scanty and have little reparative material around them. The small arteries frequently show considerable hypertrophy of their *muscular* coats. In certain cases the *inner* coat is also thickened.

FIG. 106.—PERPENDICULAR SECTION THROUGH INDURATED EDGE OF OLD INDOLENT ULCER OF LEG (×40 DIAMS.)

(*a*) Superficial dead epidermis; (*b*, *b*) granulation loops undermining and pushing up the edge; (*c*) half-organised granulation tissue beneath the edge; (*d*) accumulated mass of epidermis where thin pellicle ought to be; (*e*) pigment from blood-extravasation; (*f*) abortive granulating surface; (*g*) divided fibrous tissues of leg forming practically the floor of the ulcer; (*h*) small artery (Hæmatoxylene and Farrants' Solution).

222. **The weak ulcer** is one whose granulations are exuberant and flabby. They have a peculiarly translucent or gelatinous appearance. Masses of them may project from the wound. The cause of the wound not healing is that the granulations are too large and œdematous. The translucent gelatinous appearance which they present is due to the latter cause.

Microscopically the blood-vascular loops are seen to be long and tortuous, the fibrous reticulum of the granulations is opened out and

distended with œdematous fluid, and numerous leucocytes can be seen passing through the walls of the vessels.

Similar œdematous granulations are frequently associated with **sinuses** resulting from strumous disease of **joints**. The granulations of the wound made in excising a joint, such as the elbow, also often take on this weak œdematous appearance. Such wounds have little tendency to heal, and the cause is that the soft tissues contain many true **tubercles**. These are scattered at intervals throughout the opened out granulation tissue, and like tubercle elsewhere have a tendency to caseate. Curiously the tubercle in such cases is often confined to the granulation tissue of the wound.

223. The **varicose, inflamed,** and **sloughing ulcers** require little explanation. The first is complicated with varicose veins, the second has from some cause assumed an inflammatory character and copiously discharges thick putrefactive pus, while the third is one in which the superficial tissues on the floor have a gray sloughy appearance, and are in process of separation.

224. **Syphilitic** or **constitutional ulcers** are liable to occur in tertiary syphilitic subjects on various parts of the body, more especially where the skin is thin, as on the calf of the leg or front of the abdomen. An inflammatory pustule or tubercle first appears, this sloughs and leaves a punched-out looking vacuity with slightly elevated edges and a smooth glossy floor. They are usually multiple, and run in circles or are grouped in particular localities.

The only remarkable points that the author has found in connection with these ulcers are, firstly, that there is very little reaction of the tissues on the floor of the ulcer; and, secondly, that the small **arteries** on the floor become **obliterated** (Fig. 107). The inner coat thickens in such a manner as to constrict and finally close the lumen in many cases. An analogous thickening of the tunica intima is certainly to be seen in old ulcers of any kind, but in the above it is more universal, and goes on to total occlusion; it is a true *arteriitis obliterans*. The occlusion of the lumen probably is the **cause** of the ulceration.

FIG. 107.—GROUP OF OBLITERATED ARTERIES, FLOOR OF SYPHILITIC ULCER OF LEG (×50 DIAMS.)

(*a*, *a*) Middle-sized and small arteries entirely occluded; (*b*) congested capillary (Carmine and Farrants' Solution).

225. The **Hard Chancre**, when ulcerated, presents certain peculiarities, although there are none of them which are completely characteristic. In the infiltrated stage, before the surface has become abraded, the loose cellular tissue, such as that of the prepuce (Fig. 108), becomes densely infiltrated with small round cells. There is also a particular tendency for similar cellular exudation to accumulate in the lymphatics round the blood-vessels (*d*). The at first isolated masses of cellular exudation subsequently fuse together

and constitute a dense continuous infiltration, giving rise to the specific induration of the part. The cells are forced out chiefly on the surface, and consequently tend to push the epidermis before them. The latter becomes more and more attenuated, its cells stretched and elongated, and it finally gives way. The cellular material is then in part discharged, and a more or less complete granulating surface results. Giant cells are occasionally found in the granulations.

Klebs (No. 146, II. p. 41, 1878; and No. 104, x.) describes a **bacillus** which he has obtained from hard chancres. He produced in the monkey something like a chancre by inoculation, but it is doubtful whether it was truly syphilitic. Lustgarten (No. 46, I. 1885) found a bacillus within hard chancres very much like that of tubercle, but

FIG. 108.—PERPENDICULAR SECTION THROUGH EDGE OF HARD CHANCRE OF PREPUCE (×50 DIAMS.)
(*a*) Ulcerated surface; (*b*) epithelial edge; (*c*) dense small cell infiltration; (*d*) lymphatics encompassing an artery, filled with small round cells (Hæmatoxylene).

with this peculiarity that it is always enclosed within cells. Its length is from 3 to 4 μ and its thickness 8 μ. Two to three oval-shaped clear points, evidently spores, are contained in its interior.

Doutrelepont and his assistant Schütz (No. 43, No. x. 1885) have also described a bacillus, which is evidently identical with that of Lustgarten.

Eve (No. 59, April 10, 1886) has succeeded in cultivating on blood serum a bacillus from the blood of syphilitic patients in two instances, and from syphilitic tissues, acute and chronic, in three instances. It is characteristically beaded, and stains best with a solution of Humboldt red in aniline oil and spirit, with subsequent decolorisation by spirit.

Literature on Hard Chancre.—Consult the many works on Syphilis, and :—**Balzer :** Compt. rend. Soc. d. Biol., iii. 1886, p. 155. **Barton :** Path. and Treatment of Syphilis, 1868. **Cornil :** Syphilis (transl.), 1882. **Hutchinson :** Med. Times and Gaz., i. 1885, p. 373. **Kaposi :** Deut. Chirurg. Lief., iii. **Lee :** Holmes' Surgery, i. 1870, p. 405. **Ricord :** Lectures on Chancre (transl.), 1859. **Sigmund :** Pitha, Handbuch, i. 1869. **v. Zeissl :** Outlines of Path. and Treat. Syph. (transl.), N. Y., 1886.

226. The **soft chancre** is less densely cellular, and does not show in its early phases the same concentration of the cellular effusion around the blood-vessels. Otherwise there is not much to distinguish it from the former.

Literature on Soft Chancre.—Consult the various works on Venereal Disease, and :—**Baude :** Contribution á l'étude du Chancre Simple, 1886. **Fournier :** Practicien, ix. 1886, p. 196. **Latouche :** Bull. et mém. Soc. méd. d. Hôp., ii. 1885, p. 41. **De Lucca** (Micrococcus in) : Gazz. d. osp. Milano, vii. 1886, p. 298, *et seq.* **Sturgis :** Ashurst's Internat. Encycl. Surg., ii. 1882. **Tommasoli:** Boll. d. Soc. tra. i. cult d. sc. med. in Sienna, iv. 1886, p. 124 ; *also,* Allg. Wien. med. Ztg., xxxi. 1886, p. 351.

227. **Cancerous ulcers** are easily enough recognised when they occur in connection with a distinct tumour. Sometimes, however, the skin of various parts of the body, not unfrequently that of the front of the leg, becomes diffusely cancerous and breaks down. It then assumes very much the character of an ordinary ulcer of that part, but with this peculiarity that it does not tend to heal, or if it heals at one part it breaks down at another. If placed under favourable circumstances the wound granulates freely, and its true nature may long remain unsuspected. If the surface of the granulations, however, be scraped and the discharge examined microscopically, the cancerous character of the cells will be apparent. Large squames with prominent nuclei and occasional cell nests are abundantly prevalent.

Such ulcers are sometimes very beautiful objects when examined microscopically in section. The granulations are large, and their vessels tortuous. Among the ordinary granulation cells are to be seen numerous cell nests, and the surface is frequently covered with a delicate pellicle of squames. The side of the wound is usually infiltrated with epithelial processes derived from the rete Malpighii.

228. **Perforating Ulcer of the Feet and Hands.**—This is a peculiar form of ulcer affecting the palmar surfaces of the hands and plantar surfaces of the feet. It is usually of small size, and tends to burrow deeply, so as, in some cases, to implicate the underlying bone. The disease is commonly regarded as a neurosis, and is sometimes an accompaniment of cerebral or spinal disease, such as locomotor ataxia, but at others has no such relationship.

Pitres and Vaillard (No. 4, xv. 1885, p. 208) have examined the nerves leading to the part in a large series of cases, and have come to the conclusion that the cause is of the nature of a peripheral neuritis frequently localised to the nerves of the part affected.

Literature on Acute Perforating Ulcer of the Foot. — **Badaloni :** Bull. d. sc. med., Bologna, viii. 1881, p. 5. **Blanchard :** Paris méd., ix. 1884, p. 205. **Butlin and**

Holden: Med. Press and Circ., xxxvi. 1883, p. 6. **Chance:** Cincin. Lancet and Clinic, xiii. 1884, p. 237. **Desprès:** Gaz. d. Hôp., liii. 1880, p. 1019. **Duckworth:** Trans. Clin. Soc. Lond., xvii. 1884, p. 231. **Eve:** Trans. Path. Soc. Lond., xxxiii. 1881-2, p. 283. **Fauchon-Courtz:** Contribution à l'étude du mal perforant, 1885. **Heath:** Lancet, 1883, i. p. 452. **Henno:** Arch. méd. Belges, xxiv. 1883, p. 218. **Martin:** Considérations sur la pathog. du mal perforant, 1885. **Mirapeix:** Du mal perforant, 1883. **Monod:** Gaz. d. Hôp., lvi. 1883, p. 945. **Orsi:** Scuola med. napol, iii. 1880, pp. 16, 44. **Owen:** Lancet, 1884, i. p. 611. **Péan:** Leçons de Clin. Chir., 1883, p. 1. **Péraire:** Arch. gén. de Méd., 1886, ii. p. 26. **Pitres and Vaillard** (Alterations of nerves in): Arch. de Physiol., v. 1885, p. 208. **Polaillon:** Union Méd., xxxvii. 1884, p. 237. **Southam:** Brit. Med. Journ., 1883, i. p. 1222. **Trélat** (Spinal origin): Gaz. d. Hôp., lvi. 1883, p. 1170.

229. **Rodent Ulcer** (see "Cancerous Tumours").

Tubercular Ulceration (see "Tubercle," also "Tubercular Intestine" and "Phthisical Lung)."

Diphtheritic Ulcer (see "Diphtheria").

Methods.—For the majority of ulcerated wounds, the same as in healing by granulation (Sect. 195). If it is desired to show the organisms of the tubercular and diphtheritic ulcers, the preparation should be hardened in "A," and stained according to directions given elsewhere (see Part I., Practical Bacteriology).

General Literature on Ulcers.—Consult various text-books on Surgery and :—**Atkin:** Med. Press and Circ., xliii. 1886, p. 210. **Garden:** Brit. Med. Journ., 1882, ii. p. 1213. **Gerard:** Essai sur la pathogénie des ulceres variqueux, 1885. **Gilson:** N. dict. de Méd. et Chir. Prat., xxxvii. 1885, p. 41. **Lebrun:** Journ. de Méd., Chir., et Pharmacol., Brussels, lxxiii. 1881, p. 27. **Machi:** Arch. med. valenc., i. 1881, pp. 99, 115. **Neely:** Mississ. Valley Med. Month., Memphis, vi. 1886, p. 145. **Paget:** Holmes' Surgery, i. 1870, p. 179. **Quénu:** Rev. de Chir., ii. 1882, p. 877. **Rohe:** Atlanta Med. Rec., i. 1881-2, p. 205. **Schreider:** Contribution a l'Étude de la Pathogénie des Ulcèrs, 1883.

CHAPTER XXI

TRANSUDATIONS AND EXUDATIONS—DROPSY

THE LYMPH.

230. UNDER normal conditions, the small blood-vessels, chiefly the capillaries, are constantly allowing a certain quantity of albumin containing liquid to filter through their walls. They do so, evidently in virtue of the intravascular pressure being greater than that of surrounding parts. The liquid is poured into the numerous lymph spaces which abundantly traverse the majority of the tissues, and from these it is collected in the lymph radicles, by which again it is conveyed to the main lymphatic trunks to be returned to the blood through the thoracic duct and other large lymphatic channels. It is poured out in such quantity as to bathe the tissues, and to supply sufficient nourishment to them for their support, but in health it never tends to accumulate to excess in the part. This is effectually prevented by the lymph channels being so freely open, and also by the free absorption of the watery part, at least, of the exudation by the veins. Lymph, however, as obtained from a large trunk, does not consist simply of the liquid as it transudes from the blood-vessels. It also contains those excrementitious matters thrown off in the metabolism of the tissues. There is, therefore, one inlet by which liquid is pumped into the tissues, namely, the arteries; while there are two outlets, the veins and lymphatics, by which after having subserved its purpose it is removed from them.

Composition.—The lymph contains all the constituents of blood plasma but in proportionally different quantity. This difference chiefly lies in the fact that there is less albumin and relatively more water. It has a feeble power of spontaneous coagulation, which is aided by the addition of a piece of blood clot. Its reaction is alkaline. It has a saltish taste, and a specific gravity varying between 1012 and 1022.

RESULTS OF THE QUANTITATIVE ANALYSES OF LYMPH MADE BY VARIOUS OBSERVERS.

Analysis of the Lymph of Man.[1]

Constituents in 100 parts.	Gubler and Quevenne.		Marchand and Colberg.	Scherer.	Dähnhardt and Hensen.	Odenius and Lang.
	I.	II.	III.	IV.	V.	VI.
Water . . .	93·99	93·48	96·93	95·76	98·63	94·36
Solid matters .	6·01	6·52	3·07	4·24	1·37	5·64
Fibrin . . .	0·05	0·06	0·52	0·04	0·11	0·16
Albumin . .	4·27	4·28	0·43	3·47	0·23	2·12
Fat . . .	0·38	0·92	0·26	—	0·15	2·48
Extractive matters	0·57	0·44	0·31	—		0·16
Salts . . .	0·73	0·82	1·54	0·73	0·88	0·72

231. **Its Circulation.**—The **plasma spaces** which surround the blood-vessels on all sides do not appear to possess an endothelial lining. They are irregularly shaped lacunæ whose outline stains with silver, probably on account of their being coated with a delicate film of a cementing substance which has the power of precipitating the silver, a substance resembling that uniting endothelial cells. Although in certain localities, such as the central tendon of the diaphragm or the frog's rectum, they can be seen to lie in close relationship with the capillary blood-vessels, yet it is not likely that they actually communicate with **pores** or small openings in the latter. Under their normal amount of distension the capillary walls appear to be free from such apertures. The liquid which is transuded in reality filters through the endothelial plates, and is simply caught in the cistern-like spaces from their close propinquity.

The **lymph capillaries** are provided with a distinct endothelial wall, and the larger lymphatic trunks are constituted by their fusion. Those lymphatic trunks which are of medium size, are possessed of three tunics—an **intima, media,** and **adventitia.** The intima consists, as in the small blood-vessels, of a longitudinal fibrous coat, lined by an endothelium the nuclei of whose cells are prominent and ellipsoidal in shape. The media is made up of circular unstriated muscular tissue combined with elastic fibres, while external to this, again, is the adventitia, a loose fibrous covering, similar to that encircling the blood-vessels.

Progressively from the lymph spaces upwards to the thoracic duct,

[1] Taken from Gamgee's *Physiological Chemistry.*

the walls of the lymph channels consist first of a homogeneous cement substance, an endothelium, an endothelium and elastic tunica intima, these with a tunica media superadded, and lastly, of these with the addition of an adventitia. The adventitia contains, besides ordinary white fibrous tissue, a few longitudinally arranged unstriated muscular fibres.

The main trunks are provided with valves, a large bicuspid valve placed at the opening of the thoracic duct into the internal jugular vein, preventing the blood from regurgitating.

The natural circulation of the lymph appears to depend upon the circumstance that the pressure within the large venous trunks closely connected with the heart, into which the main lymphatic vessels open, is less than that prevailing in the tissues, and that this again is less than the pressure within the small arteries and capillaries. There is thus a constant tendency to drive the lymph upwards towards the large veins of the thorax.

There are, however, also certain accessory means by which the flow of the lymph is aided, these being mainly (1) *the contraction of the muscles;* (2) *the movements of respiration;* (3) *the contraction of the muscular coat of the lymph vessels.*

When a cannula is inserted into a main lymphatic stem, the lymph which flows from it, while the animal is at rest, is small in quantity, whereas when the **muscles** are made to contract, the amount rapidly increases. That the **movements of respiration** have a powerful pumping action on the lymphatics of the **abdomen** is proved by Ludwig's experiment upon the central tendon of the rabbit. The parts below the diaphragm are cut away in a rabbit; the thorax is inverted; and artificial respiration is kept up. A quantity of Berlin blue in suspension is now poured over the diaphragm, with the effect, that it is drawn into its lymphatics, which soon assume the appearance of a number of arborescent coloured lines.

Heller (No. 50, 1869, p. 545) described a **rhythmic contraction** of the lymph vessels of the mesentery of the guinea-pig with a tendency to push the chyle contained in them towards the central end. Foster (No. 145), however, doubts whether this is of an active nature, holding it to be more probable that it may be caused by the peristaltic contraction of the bowel tending to drive the chyle into the vessels. Special **contractile sacs** called **lymph hearts** are met with in the **frog**, and in other cold-blooded animals, but as yet have not been found in mammalia. They have the effect of driving the lymph onwards from the lymph channels into the blood-vessels.

The **lymph glands,** placed as they are in the course of the lymph vessels, have a certain filtering action upon the liquid contained within the latter, and when they are swollen by inflammatory or other products, they tend to retard the flow of lymph through the particular branches with which they are connected.

CONDITIONS UNDER WHICH ALBUMINOUS LIQUIDS ARE EFFUSED.

232. As all the proteid bodies of ordinary dropsical liquids are **colloids,** it follows that they pass through animal membranes only

under pressure. As a result of the numerous experiments made on the passage of albuminous bodies through animal membranes, the general conclusion is that they permeate through them *in amount varying as the pressure.* (Hermann, No. 186, p. 85; W. Schmidt, No. 190, p. 337, 1856, *Idem*, p. 337, 1861; Newman, No. 5, xii. p. 608, and No. 189, 1878, p. 648; Gottwalt, No. 187, p. 423; Bamberger, No. 188, 1881).

Runeberg, however (No. 140, xxiii.; No. 126, xviii.; and No. 169, xxxv.), employing the intestine toughened in alcohol as the experimental membrane, arrived at results differing materially from those generally accepted. With a **fresh** or **rested membrane** under a pressure of one mètre water, he found that the relative amount of albumin in the filtrate increased with the time until a certain point was reached at which it became constant. As soon as this constant stage is attained, the albumin of the filtrate *diminishes by raising and increases by diminishing the pressure.* The amount of albumin also which passes through a membrane, is greater if the membrane is allowed to rest for a while than when the pressure is constant.

There are certain serious objections to applying these results in explanation of the transudation of albumin through a capillary vessel. One of the most evident is that the intestine is a *compound* membrane formed of different coats whose fibres interlace almost at right angles to each other. Hence, under increased pressure, the solid parts of the one are liable to be driven into the pores of the other, and in this way the membrane might be rendered less pervious; whereas a relaxation of the pressure, by freeing the impaction of the one against the other, would tend to allow more liquid to pass.

This will hold good with still greater reason if we accept Runeberg's hypothesis that solutions of albumin are mere **emulsions**, the small particles of albumin being suspended in the water. One can easily see how, when the pores of the membrane become clogged with these, a relaxation of the pressure will favour a greater quantity of albumin passing through, while an increase will diminish it.

In point of fact, all experiments on dead membranes of this kind taken alone, when applied to the explanation of the phenomena of transudation from the living vessels, are untrustworthy. If we want to get at reliable results, they must be controlled by experiments upon the living animal.

DEFINITION OF DROPSY.

233. A certain quantity of lymphy liquid is constantly being effused into the tissues and serous cavities of the body, but in the case of the latter it is never more than sufficient to keep them moist. When any excessive accumulation takes place, the condition is known as **Hydrops**, or **Dropsy**, and the liquid effused is known as a **Transudate** or **Exudate**, according to circumstances. A "transud-

ate" is such a liquid having a composition resembling that of the blood serum, while the term "exudate" is usually applied to an effused liquid whose composition approaches that of the blood plasma in the relationship of its solid and liquid parts, and which, besides, usually contains numbers of colourless blood corpuscles (compare Perls, No. 170, i. p. 49). The former is what is commonly found in *dropsies*, the latter is more frequently the effect of an *acute inflammation*. As we have already discussed the character of inflammatory effusions (Chap. xix.), it will be with the former of these alone that we shall now have to deal.

GENERAL CAUSES OF DROPSY.

234. The natural means of circulating the lymph being those just described (Sects. 23, 231), how is it that an excessive accumulation, a lymph congestion or dropsy, is caused? There are several possibilities, the chief of which are the following:—(1) *Increased arterial pressure;* (2) *arterial dilatation;* (3) *obstruction in the venous outlets;* (4) *obstruction in the lymph channels and glands;* (5) *obstruction to both veins and lymphatics;* (6) *alterations in the walls of the capillary blood-vessels;* (7) *an undue laxity of the tissues;* or (8) *a wrong composition of the blood.* Let us see in how far each of these is instrumental in its production.

235. (1) **Increased Arterial Pressure.**—It might be supposed, and the old idea was that ligature of a large peripheral arterial trunk raises the general arterial pressure. Such, however, is usually said not to be the case. If a manometer be placed in the carotid of a dog, and a ligature be applied to the femoral artery, with the exception of a slight elevation of the pressure at the moment of ligature, no general augmentation takes place. If the aorta be ligatured *below* the renals, no general rise of the arterial pressure occurs. It is only when the aorta is ligatured at a point higher than this that any material rise in the arterial pressure is noticed (Cohnheim).

It has further been shown by Lichtheim (No. 172), that the pressure within the *pulmonary system of vessels* appears to be in great part independent of that in the *systemic arteries*. If the branches of the pulmonary artery be ligatured so as to narrow their circulating capacity by three-fourths of their entire extent, the pressure within the open branches of the pulmonary artery certainly rises, but this has little, if any, effect upon the pressure within the carotid artery. The pressure within the carotid can be conversely raised to double its natural height without materially influencing that of the pulmonary artery.

The chance of morbidly increasing the general arterial pressure throughout the body by mechanical obstruction to the circulation through any particular system of arteries may, therefore, practically be placed out of consideration.

Even if it were appreciably raised in a particular set of arteries, there are good grounds for believing that so long as the venous chan-

nels are freely open, an **œdema** of the part from this cause would not result. Thus (Cohnheim, No. 31, i. p. 419), when, in a rabbit or dog, the left chief branch of the pulmonary artery is ligatured along with the branch of the right going to the upper lobe, or when three-fourths of the larger pulmonary artery branches are occluded by embolism, œdema of the lung does not follow.

Even **increased contractile power** in the heart seems to have no effect in causing œdema. So long as the venous outlets are free, the blood pressure apparently does not rise, and œdema is consequently not induced.

236. (2) **Arterial Dilatation.**—If the afflux of blood to a part be increased by dilatation of the arteries, will this call forth a dropsy? The majority of the experiments bearing upon the subject have been made by inducing arterial dilatation either by division of the **vaso-constrictor** nerve trunks or by irritation of the **vaso-dilators.**

It is a well-known fact that in certain neuro-paralytic affections there is a great tendency to dropsy of the extremities. Strubing (No. 91, ix. p. 381, 1885) supposed that in some of these cases there may be an increased excitability of the vaso-dilators. In those who have sustained a fracture of the spine, with compression of the cord and resulting paraplegia, œdema of the lower extremities is a common symptom.

Division of the sympathetic in the neck of the rabbit is followed in course of time by an **enlargement of the corresponding ear.** Whether this is owing to an **œdema** caused by the paralytic vascular distension, or whether it is a true **growth** of the tissues due to the increased supply of blood, is not quite clear. The latter view is the more probable.

Jankowski (No. 13, xciii. p. 259, 1883) made out that after inflaming the hind paws of a dog and dividing the sciatic nerve on one side, the quantity of lymph returned from the limb in which the division had been practised, as well as the amount of œdema in that limb, was considerably greater than in the opposite.

In dogs rendered artificially *hydræmic*, Salvioli (No. 49, i. p. 252, 1885) found that dropsy ensued only in the limb in which the sciatic had been divided.

Ostroumoff (see reference by Brunton, No. 173, p. 340) found that when the **lingual nerve** is irritated, not only do the vessels of the tongue dilate, but the whole side of the tongue becomes œdematous.

When the chorda tympani is stimulated, a copious secretion of watery saliva occurs, along with dilatation of the blood-vessels of the gland (C. Bernard, No. 40, 1862). Brunton (No. 173, p. 341) looks upon this excessive secretion as due to the lymph spaces of the gland becoming loaded with dropsical liquid which the secreting cells take up in excess.

In all these cases, however, the dropsy has been the result of an *abnormality in the nerve supply of the part*, and hence there may be a cause at work other than the purely mechanical *arterial dilatation.* The relaxation of the muscles, for instance, and the consequent hindrance to the onward flow of the lymph in a paralysed limb, might be an important factor in its production.

237. (3) **Obstruction to the Venous Outlets.**—Of all known factors this is one of the most powerful in bringing about a local

dropsy. It must be remembered, however, that the effect of occluding the venous outlets, either completely or partially, appears to depend upon the *particular venous circle* which is obstructed.

As a matter of clinical experience, we know that when the portal blood is hindered in its transit through the liver, as by a **cirrhosis** or other obstruction, a dropsy confined to the abdomen is a common result. The portal ramifications on the abdominal organs are found in such cases engorged with blood, and there seems little doubt that the causation of the dropsy is purely obstructive.

When some of the larger branches of the portal vein in entering the organ become occluded by disease, the capillaries in connection with those which are still pervious become so dilated within the liver substance as to give rise to an appearance resembling that of an angeiomatous tumour.

When, on the contrary, the **mitral** becomes **stenosed** so as to narrow the orifice and thus hinder the return of blood from the lung, the small veins and capillaries of the lung become similarly dilated. It by no means follows, however, that the lung will be found to be **œdematous**. It is usually in the condition known as "brown induration," but many of these lungs are peculiarly *dry*. Œdema may be met with in such cases, but not constantly, and it is quite possible that the liquid when present, may have been effused as the heart's action became weakened during the agony.

Welch (No. 13, lxxii. p. 392) found that when the pulmonary circulation was obstructed by ligaturing the aorta close to its origin, an œdema of the lung was certainly forthcoming, but that the blood-pressure required to be raised to a pitch far beyond what would ever occur in Man before this result was attained. In direct ligature of the pulmonary veins, he also found (pp. 398 and 400) that nearly the whole of the venous outlets must be occluded before œdema of the lung resulted.

It appears likely that the explanation of his results resides in the fact that the capillaries ramifying on the alveolar wall are so readily distensile that they can hold a large quantity of additional blood without having their pressure materially altered. The thin layer of epithelium which alone covers them on one side, together with the negative intra-alveolar pressure during inspiration, will tend to encourage this accommodating faculty.

When the inferior vena cava is ligatured above the diaphragm in the dog, as shown by Richard Lower more than two hundred years ago (No. 174), an ascites follows. When the inferior vena cava is ligatured lower down, an œdema of the posterior extremities sometimes follows, but more often does not. Ranvier (No. 40, lxix. No. 25, 1869 ; see also Hehn, No. 50, No. xl. 1873), has shown, however, that when the cava is ligatured, and when, in addition, the vaso-motor nerves going to the hind limbs are divided, œdema is a much more regular effect. Where the vein alone is ligatured, the blood is evidently capable of

being returned by anastomotic paths. Where the vaso-motor nerves are also divided, the afflux of blood through the paralysed arteries is so great that these compensatory channels are incapable of removing it and an obstructive œdema results (Sotnischewsky).

Brunton (*loc. cit.* p. 331), is inclined to differ from this which is the usual explanation, and would regard the absence of œdema in simple ligature as an effect of increased action of the lymphatics. Ludwig (No. 46, 1863) found that when a part is rendered artificially œdematous, by placing a ligature round the upper lip, the neighbouring lymphatics carry off a great bulk of the effusion when the ligature is removed.

However this may be, the fact holds good that **ligature** of a **single vein** returning from a limb has little, if any, effect in inducing an œdema. When, however, **several branches** are occluded, as by the injection into them of plaster of Paris (Sotnischewsky, No. 13, lxxvii. and Jankowski, No. 13, xciii.), a local œdema is the usual result. When the branches of the femoral vein are occluded in Man by a **thrombus**, a similar œdematous swelling of the lower extremity follows (*phlegmasia dolens*).

238. (4) **Obstruction in the Lymph Channels and Glands.**—Where the **thoracic duct is obstructed** to occlusion by the pressure of tumours or from other causes, the peripheral portion becomes varicosely dilated, more or less ascites results, and sometimes the receptaculum chyli may rupture (see Chylous Dropsy, Sect. 256). When a **local set** of lymphatics is **obstructed by ligature**, or when the **lymphatic glands** in connection with them are **excised**, dropsy does not follow so long as the transudation from the vessels remains normal. The veins seem capable of functionally replacing the lymphatics in removing the liquid effused into the tissues. (See Cohnheim, No. 31, i. p. 408; also v. Dusch, No. 126, vi. 1861.) **Collateral lymph channels** are soon opened up which serve to carry on the absorptive function of the part as before.

239. (5) **Obstruction both in Veins and Lymphatics.**—Where both the veins and lymphatics are obstructed, however, as by applying a ligature round a limb, a copious local dropsy sets in; and this, according to Sotnischewsky (*loc. cit.*), is independent of whether the vaso-motor nerves are divided or not.

240. (6) **Alterations in Walls of Capillary Blood-vessels.**—This is admitted by all pathologists to be a most important factor in the production of a certain class of dropsies. When we consider how thin and delicate the capillary wall is, we can easily see that a slight alteration in its endothelial plates would render the transudation of liquid easier than in health.

The experiment which has the most direct bearing on this subject is that of the stimulation of the chorda tympani in an animal poisoned by atropine (Heidenhain, No. 169, v. p. 309). The sub-maxillary gland becomes congested, but neither is there an increased secretion

from its gland cells, nor is the quantity of lymph which drains away from the lymphatic trunks of the neck at all increased. The gland cells cease to secrete, and the vessels of the gland, although they become distended, fail to allow the liquid to escape from them.

The usual **explanation** given of this experiment is that the atropine **paralyses** the **secreting nerve twigs**, and hence puts a stop to the flow of saliva. This would not, however, account for the absence of œdema in the gland. Brunton (*loc. cit.*, p. 342) explains it on other grounds, namely, that the atropine has some direct and immediate action upon the tissues of the vessel walls whereby their power of allowing the liquid part of the blood to exude is abolished.

Gaskell (see No. 173, p. 343) has shown that **dilute acids** cause relaxation of the muscular substance both of the heart and blood-vessels, while dilute alkalies have an opposite effect. Brunton and Cash (No. 173, p. 343) have observed that not only do the vessels dilate under the influence of acids added to the blood, but that the tissues become œdematous from the increased transudation through the walls of the former; and they think it probable that the cause of this is an alteration effected by the acid whereby the coats of the vessels are rendered more permeable. There is also a strong belief (Cohnheim, Lister, and others), that in **inflammation** there must be some marked alteration in the walls of the vessels allowing of the increased transudation, and probably accounting for several other phenomena.

241. (7) **An undue Laxity of the Tissues.**—There cannot be much doubt that the less resistant the tissues surrounding the small blood-vessels, the more likelihood will there be of any unduly great vascular pressure causing an increased transudation of liquid. We see this borne out in the fact that soft areolar tissues, such as those of the eyelids, backs of the hands and feet, and scrotum, become dropsical in preference to hard dense tissues, such as muscle, bone, and tendon.

Landerer (No. 113) holds, on the principles previously explained (Sect. 194), that the commonest cause of dropsy is the loss of the elasticity of the tissues along with an alteration in the walls of the vessels. This loss of the natural counterpoise of the tissues may be the result of a long-continued distension of the vessels. Brunton (*loc. cit.*) calls attention to the fact mentioned by Ludwig that short-haired dogs afford more lymph than those which are long-haired, and accounts for it by their muscular fasciæ being much more rigid, and hence forcing out a greater amount of lymph each time the muscle contracts. The lymph has not such a tendency to accumulate in them as in an animal with lax tissues, and probably the same laxity carried to an extreme may at least aid in producing certain dropsies.

242. (8) **A wrong Composition of the Blood.**—Cohnheim and Lichtheim (No. 13, lxix. p. 106) found that when dogs are rendered artificially hydræmic by injecting large quantities of 0·6 per cent salt solution into the blood-vessels so as to produce a **hydræmic plethora**, the quantity of fluid exudation which is given off into several organs is markedly increased. It makes itself first appreciable by an increase of the stream issuing from the lymphatics and in course of time by infiltrating the meshes of the tissues of the organs affected. The organs which are the subject of this œdema, however, are not

those which are the usual seat of general dropsy such as that from disease of the kidney. On the contrary, these remain free from œdema, while those which become hydræmic (pancreas, kidney, spleen, lymph-glands, gall-bladder, retro-peritoneal cellular tissue, and connective tissue of salivary glands, etc.), are exactly those which are excepted in dropsy from renal disease. Neither the pericardial sac nor pleural cavities contain any excess of liquid; the lungs are unusually dry; but the connective tissue spreading out from the hilus pulmonis is slightly swollen and œdematous. These observers concluded (p. 137) that neither **hydræmic plethora** nor **hydræmia** can account for the œdema of renal disease.

It might be supposed that the extra liquid was shed by the kidneys which thus acted as a safety valve. Fleischer (No. 175, No. I. July 1885), in order to test the validity of this objection, first tied the ureters, and subsequently injected large quantities of neutral liquid into the circulation. He found that the **blood pressure** was not permanently raised, and that there was no anasarca. The addition of urea to the liquid made no difference.

Œdema of Skin in Hydræmia.—A curious point is that in such experiments on dogs the skin does not become œdematous, and Salvioli (No. 49, No. I. 1885, p. 252) explains it on the supposition that the skin of the dog is less permeable to water than that of Man. It seems probable, however, that the œdema of the skin in human renal disease may in part be due to the long-continued stretching of the tissues.

In all these experiments, moreover, on dogs, the animal was allowed to live only a few hours. The œdematous stretching of the skin is a comparatively slow process in œdema from renal disease. The skin of the dog may, likewise, be more resistant than that of Man, and hence would require a more prolonged effort to stretch it.

Cohnheim and Lichtheim (*loc. cit.*) supposed that the skin in renal disease and in the various cachexiæ accompanied by dropsy may be in a morbid state. They assumed that in the hydræmia of renal disease, anæmia, and so on, where there is a wrong composition of the blood, the vessel walls must generally be in a state favourable for the increased transudation of liquid, and that those of the skin are similarly debilitated. They thus regarded the œdema in such cases not so much as directly dependent upon hydræmia as upon this increased permeability of the vessel walls.

A common form of dropsy is that resulting from extreme **anæmia**, and here it is at any rate probable that the nutrition of the walls of the vessels is insufficiently supported, and that on this account they allow an increased transudation.

Hydræmia and Division of Sciatic.—According to Salvioli (*loc. cit.*), division of the sciatic nerve in artificially hydræmic dogs, renders the corresponding limb œdematous. How this comes about may be open to question.

Alteration in Specific Gravity of Blood.—There may be, however, another explanation of the œdema which accompanies an alteration in

the composition of the blood, namely, that being of improper specific gravity, it increases the difficulty in circulating the blood corpuscles, and hence tends to increase the whole vascular tension and to press out a greater quantity of water than usual (see "Albuminuria.")

General Literature on Dropsy.—**Baur**: De la Pathogénie des Hydropisies, 1877. **Bergeon**: Des Hydropisies en général, 1852. **Bouillaud**: Gaz. d. Hôp., liii. 1880, p. 20. **Bright (R.)**: Reports of Med. Cases, 1827, p. 31; *also*, Guy's Hosp. Rep., 1836. **Brochin**: Gaz. d. Hôp., xlvii. 1874, p. 177, *et seq.* **Christison**: On Granular Degeneration of the Kidneys and its Connection with Dropsy, 1839. **Colin**: Bull. Acad. de Méd., viii. 1879, p. 1283. **Colleville**: Essai sur Quelques Variétés d'Anasarques sous Albuminurie, 1885. **Cordier**: Des Hydropisies en général, 1846. **Courtois**: De l'Hydropisies en général, 1854. **Davidson** (Epidemic D.): Edin. Med. Journ., xxvii. 1881-2, p. 118. **Hartmann**: Berl. klin. Wochnschr., xxiii. 1886, p. 612. **Johnson**: Lancet, 1864, i. p. 59; *also*, Brit. Med. Journ., 1868, i. p. 213. **Laycock** (Nervous Influence): Edin. Med. Journ., xi. 1866, pp. 775, 895. **Reilhac**: Des Hydropisies en général, 1847. **Senator**: Arch. f. Path. Anat., cxi. 1888, p. 219. **Sharkey**: Med. Press and Circ., vi. 1868, pp. 505, 524. **Smith** (Acute Œdema): Ind. Med. Gaz., Calcutta, xiv. 1879. **Straus**: N. Dict. de Méd. et Chir. prat., xviii. 1874, p. 33. **Strelzoff**: Acad. de Sc. de Montpel. Mem. Sect. méd., iv. 1864, p. 163. **De Veseaux, De Laveryne**: Étude critique sur la Pathog. des Hydropisies, 1873. **Virchow**: Handbuch d. Spec. Path. u. Therap., i. 1854. **Wagner**: General Pathology (Eng. transl.), 1877, p. 224.

Literature on Etiology of Dropsy.—**Adam**: Altérations des solides et des liquides qui peuvent produire les hydropisies, 1880. **Barr**: Med. Press and Circ., xli. 1886, p. 491; *also*, Path. and Treatment of Dropsy, 1886. **Bernard (Cl.)** (Artificial Hydræmia): Compt. rend. Soc. d. Biol., 1849. **Boddaert**: Ann. Soc. de méd. de Gand., liii. 1875, p. 209. **Boragine**: Gazz. med. ital. prov. venete, xiii. 1870, p. 393. **Bott**: Berl. klin. Wochnschr., xi. 1874, p. 100. **Cobleich** (Nervous): Med. and Surg. Rep., Phila., xxxvi. 1877, p. 74. **Declaux**: De l'étiologie des hydropisies, 1855. **v. Dembowski**: Ueb. d. Abhängigkeit d. Œdema v. Hydraemie, etc. 1885. **Denis**: Des causes de l'hydropisie, 1852. **Dutrochet**: Nouvelles recherches sur l'endosmose et l'exosmose, 1828. **Gaillard**: Sur la pathogénie des hydropisies, 1863. **Hehn**: Centralbl. f. d. med. Wissensch., xi. 1873, p. 625. **Hernandez-Hevia**: Étude sur l'ascite l'anasarque et l'œdème, 1857. **Lebert** (Artificial Hydræmia): Compt. rend. Soc. d. Biol., 1849. **Lefeuvre**: De l'étiologie des hydropisies, 1851. **Lewald**: Beitr. z. Theorie d. Enstehung d. Œdeme, 1885. **Mathiew**: Arch. gén. de méd., 1885, i. p. 656; *Ibid.*, 1885, ii. p. 171. **Moucade**: Étude sur l'étiologie de l'ascite, 1874. **Le Noir**: Essai sur la pathogénie de l'ascite, 1875. **Schmidt**: Ann. d. Chemie u. Phar., 1848. **Sée**: Leçons de pathol. expérimentale, 1866.

CHAPTER XXII

TRANSUDATIONS AND EXUDATIONS—DROPSY—(*Continued*)

DROPSIES OF SPECIAL PARTS.

243. **Nomenclature.**—According to the tissue or cavity in which the dropsical liquid has accumulated, special designations are correspondingly employed. Where the dropsy is more or less general the condition is known as **anasarca** (ἀνά and σάρξ, flesh). If the tissues are locally infiltrated, as where the eyelids, lung, or scrotum are the only seat of it, the term **Œdema** (οἰδέω, to swell) is usually applied.

A collection of dropsical liquid within the pleura is known as a **hydrothorax** (ὕδωρ, water); that within the pericardium as a **hydropericardium**; and that within the abdomen as an **ascites** (ἀσκός, a sac) or **hydroperitoneum**. A distension of the ventricles of the brain is termed a **hydrocephalus** (κεφαλή, the head); and where a congenital deficiency exists in the skull, and the membranes distended with liquid are protruded through it so as to form a tumour, the condition is known as a **meningocele** (μῆνιγξ, a membrane, and κήλη, a tumour); where, in addition to the membranes, the tumour contains a thin layer of brain substance, the term **hydrencephalocele** (ἐγκέφαλος, the brain) is employed. Distension of the central canal of the spinal cord is known as a **hydrorachis** (ῥάχις, the spine); a dropsy of the tunica vaginalis as a **hydrocele** (κήλη, a tumour); that of the eyeball a **hydrophthalmus** (ὀφθαλμός, the eye); while a dropsical over-distension of the womb receives the name **hydrometra** (μήτρα, the womb), and that of the Fallopian tube **hydrosalpinx** (σάλπιγξ a tube). Dropsy of the ureter, pelvis of the kidney, and calices is called a **hydronephrosis** (νεφρός, the kidney); and that of a joint a **hydrarthrosis** (ἄρθρον, a joint).

244. **General Œdema or Anasarca.**—The tissues which become most distended are those which are loosest in texture. The eyelids, particularly the lower, the scrotum, the backs of the hands and feet, and the areolar subcutaneous tissues on the front of the trunk are the particular localities in which it is to be first looked for, and in which

the liquid tends mostly to accumulate. The areolar fibrous tissues become opened out and their interspaces filled with liquid. The connective tissue nuclei tend to be shed from the bundles on which they lie, and become more prominent objects than previously, while the fat is in part absorbed. The superficial layers of epidermis are separated from the deep, and are sometimes thrown up in blebs, and in the event of the lung being simultaneously œdematous, the epithelium of the alveolar cavities and that of the small bronchi is extensively shed.

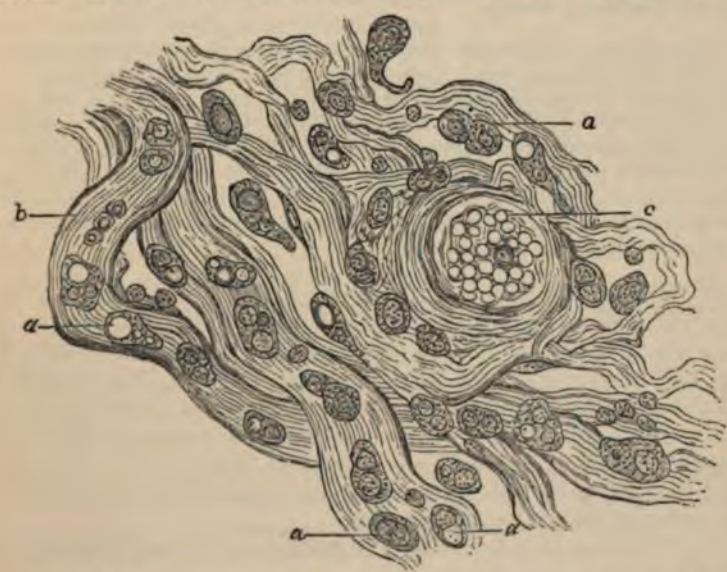

FIG. 109.—ŒDEMATOUS PERIBRONCHIAL FIBROUS TISSUE OF LUNG (× 450 DIAMS.)

(*a*) (*a*, *a*, *a*) Connective tissue corpuscles, desquamated and vacuolated; (*b*) bundle of white fibres; (*c*) congested vessel (Picro-carmine and Farrants' solution.)

The causes of anasarca must, of course, be more or less general. Renal disease, or renal disease accompanied by a cardiac valvular deficiency, is by far the commonest. Minor degrees of it occur in anæmia whether or not connected with some dyscrasia.

In warm climates a general anasarca sometimes comes on suddenly during the rains. It affects both natives and Europeans.

245. **Local œdema** may be due to so many different causes, that it is impracticable to refer to them here in a systematic manner. Some of the more specialised local œdemas are: (1) The *Lymph Scrotum* and *Lymphatic Œdema of the Leg* or Elephantiasis lymphangiectodes of tropical and subtropical climates. This disease appears to be associated beyond doubt with the parasite known as the **filaria sanguinis hominis** (see "Animal Parasites," vol. ii.) The explana-

tion given by Lewis (No. 177), Manson (No. 176, xiii. 30; xiv. 1; xviii. 31; xx. 13), and others of the cause of the disease is that the lymphatic vessels and lymph glands become occluded through the presence of the parent parasite, the embryos, and the ova.

The scrotum or leg, as the case may be, is much swollen, and the bundles of areolar tissue become widely separated by irregularly-shaped spaces, filled with albuminous liquid, containing a few lymph corpuscles and the embryo parasites. These spaces are in reality dilated lymphatic vessels.

As to whether the obstructive theory, above referred to, be tenable or not, there may be some difference of opinion. From experimental evidence already quoted (Sect. 238), it seems that the obstruction of the entire lymphatic trunks of a limb alone is not sufficient to cause œdema. Whether a *continuous* and *progressive* plugging of these by the embryo parasites, extending over many months, may not bring about the result, seems as yet not to have been disproved. The new lymph paths opened up as the old ones become occluded might successively become obstructed by fresh filariæ getting into them, whereas in the ordinary experiment of ligaturing the lymph channels the conditions are different.

(2) *Œdema due to Trichinæ.*—Another form of local œdema due to a parasitical cause, is that which follows in the face and limbs from the invasion of the **trichina spiralis.** It has been asserted that the affection is due to an obliteration of the capillary vessels of the muscles in which the trichinæ become embedded (Colberg). It has also been suggested that the lymphatic channels become plugged with them, and the lymph stream thus obstructed (Klob). Later researches seem to point to the œdema being of an inflammatory nature, due to the irritation caused by the parasites.

(3) The cause of œdema from the **poisonous bites of insects or stings** is as yet unexplained.

Literature on Local Œdema.—**Carrieu and Francois:** Gaz. hebd. d. sc. méd. d. Montpel., iii. 1881, pp. 61, 121. **Chossat:** Sur les conditions pathogéniques des œdèmes, 1874. **Fleischer:** Sitzungsb. d. phys. med. Soc. zu Erlang., 1883-4. **Hadden:** Lancet, 1886, i. p. 1212. **Hervonet** (Unilateral): Gaz. méd. de Nantes, iv. 1885-6, p. 15. **Hesse** (Bacilli in Malignant O.): Deut. med. Wochnschr., xi. 1885, p. 214. **Hutchinson:** Lancet, 1876, ii. p. 281. **Ranvier** (Connective T. in O.): Compt. rend. Acad. d. Sc., 1871. **Rathery:** Pathogénie de l'Œdeme, 1872. **Salvioli:** Lond. Med. Rec., xix. 1885, p. 59. **Strübing:** Ztschr. f. klin. Med., ix. 1885, p. 381.

246. **Hydrothorax.**—The liquid which accumulates in the pleural cavity is usually clear and serous. After death a few flakes of fibrin may be occasionally seen in it, but these are probably not present during life. The thoracic viscera are compressed by the liquid, the lung collapsed, flattened like a placenta, and it may be so devoid of air that a portion cut off sinks in water. The lung itself under such circumstances is not œdematous.

247. **Hydropericardium.**—The quantity of liquid naturally present in the pericardial sac is very small, not more after death than a drachm to a drachm and a half. In dropsy of the sac it may accumu-

late to the extent of many ounces, the sac becoming distended and the percussion dulness increased. When the quantity of liquid is comparatively small (15 oz., Sibson) the sac assumes a pear shape with the broad end downwards, when in greater quantity ($3\frac{1}{4}$ lbs.) it becomes more of an obtuse cone, the base downwards as before. The broad attachment of the sac to the central tendon of the diaphragm and its narrow extremity superiorly where it expands upon the aorta and pulmonary artery, give the sac naturally a somewhat conical shape, and this is retained when it is distended with liquid. The percussion dulness roughly corresponds to this shape.

248. **Ascites.**—The liquid here may also sometimes contain a little fibrinous precipitate after death, but rarely during life. It has usually a citron-yellow or greenish colour. In the upright position of the body, fluctuation is readily felt when the abdomen is compressed on the one side and lightly tapped on the other. When the body is horizontal, however, such a distinct sign of the presence of liquid can be with difficulty elicited, and the intestines float up to the highest level.

Literature on Ascites.—**Arnauld:** De l'Ascite a frigore et de l'Ascite rheumatismale, 1874. **Besnier:** Dict. Encycl. d. sc. méd., vi. 1867, p. 435. **Bristowe:** Reynolds' Syst. Med., iii. 1871, p. 260; *also*, Diseases of Intestine and Peritoneum, 1879. **Caucanas:** Sur la Pathogenie, etc. de l'Ascite, 1875. **Dumas:** Gaz. Hebd. d. Sc. Méd. de Montpel., vii. 1885, p. 40. **Habershon:** Lancet, 1867, i. pp. 535, 562. **M'Donald:** Med. Rec. N. Y., xxviii. 1885, p. 513. **Murchison:** Lectures on Diseases of the Liver, Jaundice, and Abdominal Dropsy. **O'Brien** (Acute Dropsy): Indian Med. Gaz., Calcutta, xiv. 1879, p. 127.

249. **Hydrocephalus.**—In acute meningitis a quantity of liquid is, as a rule, poured out into the ventricles and into the spaces between the membranes. This cannot be regarded, however, as a dropsy proper, as there is usually an effusion as well of more or less inflammatory lymph and even pus within the membranes at the base, or in some other locality. (For further particulars see "Acute Meningitis.")

True dropsy of the brain and its membranes is usually of more or less chronic origin, and is frequently congenital; if not congenital, it supervenes in the early months of infancy. It is particularly liable to occur in rickety children.

It has been described as *internal* and *external* (Virchow), according as the ventricles or the spaces between the membranes are the seat of the dropsical effusion.

Hydrocephalus internus.—*Anatomical Description.*—If the subject of the disease be an infant, the head will be found to be of enormous size, the fontanelles and sutures of the bones of the skull widely open, the scalp thin and stretched, and the face when compared with the head unusually small. The bones of the skull are thin and diaphanous, the convolutions of the brain flattened, and the sulci opened out and shallow. The veins on the surface of the brain are, as a rule, compressed, and contain little blood, and the amount of liquid in the subarachnoid space is small in quantity. The accumulation has

essentially taken place in the ventricles, which are converted into one huge common sac.

It will be remembered that the division of the ventricular system of the brain into the two lateral and the third, is a purely arbitrary one, and is brought about simply by the corpus callosum and fornix being pushed downwards, as it were, and thus constituting an incomplete partition. The foramen of Monro is nothing more than the continuity of the common cavity at each side of the fornix (see Fig. 8, Sect. 21). If, therefore, the fornix with the corpus callosum lying above it, were driven upwards, and moreover, if the septum lucidum were driven forwards, the three ventricular cavities would become converted into a common space. This is what actually happens in hydrocephalus. The **fornix** and **corpus callosum** are forced *upwards*, and become stretched to such an extent that they may be actually destroyed, or so attenuated that they look like a thin sheet of parchment. The **foramen of Monro** consequently becomes annihilated. The **septum lucidum**, with its attached descending **pillars of the fornix,** is driven forwards and flattened, while yet additional space is gained by the compression of the **basal ganglia.** The latter are hardly recognisable, as they cause almost no projection on the floor of the cavity. The **tuber cinereum** is extremely thin and transparent, in fact in many cases it can hardly be said to exist. The **velum interpositum,** and the **choroid plexus** lie free in the liquid, and are not, so far as the author has seen, of large size, nor are their vessels unusually congested. The **cortical gray matter** of the organ and the subjacent **white matter** are so attenuated that absolutely in some places there appears to be little left except the membranes, blood-vessels, and connective tissue.

It will be remembered that the **common ventricular cavity** communicates with the fourth ventricle, by the aqueduct of Sylvius. The latter is usually so distended that it will readily admit a goose quill, sometimes the little finger. The **central canal** of the spinal cord need not necessarily be distended. The **walls of the ventricles** are usually covered with the so-called **granulations,** so frequently seen in various chronic diseases of the brain (vol. ii.). The **anterior commissure** is not destroyed, but lies exposed on the floor of the cavity. The ependyma may be considerably thickened as if from organised lymph.

The **quantity of liquid** contained in the cavity is sometimes truly enormous. From a child two weeks old the author has known as much as 75 ounces to be withdrawn after death.

Causes.—This subject is so complicated that it would be injudicious to say much about it. There are so many possibilities, and so few facts to support any of them that it would require much definite experimental evidence to arrive at anything like satisfactory conclusions. Thus the **venous return** by the veins of Galen or by the sinuses may be obstructed, and so induce an unusual exodus of liquid. Although

cases have been recorded in which some obstruction in the venous return has been apparent, yet in the majority of instances nothing of this kind has been detected.

A too **great yielding capacity** of the cranial vault might be regarded as another evident cause, and the rickety habit of the subjects of hydrocephalus lends countenance to it, as well as the fact that the liquid ceases to increase in quantity when ossification of the bones of the skull ensues. Whether this alone, without any obstruction in the venous outlets, is sufficient to induce the distension, may legitimately be questioned.

Fatality.—The greater number of children affected with hydrocephalus die in infancy or during the first few years of life. A considerable number, however, reach adolescence, even where inspection of the parts after death reveals such atrophy of the cerebral hemispheres as might well be supposed to be incompatible with life.

Hydrocephalus Externus.—The liquid here accumulates in the sub-dural and sub-arachnoid spaces, but chiefly in the latter. The pia mater and arachnoid are naturally united by numbers of trabeculæ of fibrous tissue, between which are intervals filled in health with cerebro-spinal liquid. The spaces are lined with endothelium, and are to be regarded as so many lymph cisterns or receptacles. These and the sub-dural space become more or less distended in this form of hydrocephalus.

Causes.—The usual cause of the disease is a **shrinking** in some of the cranial contents, manifestly in the tissue of the brain itself. The cerebro-spinal fluid normally fills all the vacuities not occupied by the cranial viscera, and, accordingly, if the latter decrease in bulk, the former will correspondingly increase. In **old age** a shrinking in the size of the brain takes place, and hence this is one of the commonest factors in the production of the condition. It is said that chronic **drunkards** are liable to a similar distension of the sub-arachnoid space, but this statement should be accepted with caution. A loss of brain substance sometimes supervenes on **embolism, hæmorrhage,** etc. As the dead brain tissue becomes absorbed, a localised **porencephalous** condition follows, in which the vacuity is occupied by loose trabeculæ of fibrous tissue filled with liquid.

Literature on Hydrocephalus.—**Adamkiewicz** (Brain Pressure—experimental): Sitzungsb. d. k. Akad. d. Wissen. Wien., lxxxviii. H. 1, Ab. 3, 1884, p. 11. **Ahlfield:** Die Missbildungen d. Menschen, Ab. ii. 1882. **Arndt:** Arch. f. path. Anat., lii. 1871, p. 42. **Begbie and Haldane:** Edin. Med. Journ., 1855-6, i. pp. 718, 751; *also in* Select. of Works of former, 1882, p. 83. **Belt:** Boston Med. and Surg. Journ., lxxxiv. 1871, p. 110. **Bouchut:** Paris méd., ix. 1884. **Bouillaud:** Gaz. d. hôp., xxxv. 1862, p. 2. **Chopin:** Am. Med. Times, N. Y., vi. 1863, p. 124. **Dickinson:** Lancet, 1870, ii. p. 73 *et seq.* **Edmunds:** Trans. Path. Soc. Lond., xxxii. 1880-1, p. 4. **Forcheimer:** Journ. Am. Med. Assoc., Chicago, iv. 1885, p. 285. **Gaggel:** Der Hydroceph. u. d. Hydrorrhachis, 1868. **Griffith:** Treatise on Hydrocephalus, 1835. **Huguenin:** Handb. d. spec. Path. (v. Ziemssen, suppl. Bd.), p. 1. **Kent:** Chicago Med. Times, xi. 1879-80, pp. 372, 417. **Leber:** Arch. f. Ophth., xxix. 1883, p. 273. **Minot:** Syst. Pract. Med. (Pepper), Phila., v. 1886, pp. 740, 723. **Newman:** Glasg. Med. Journ., xviii. 1882, p. 161. **Prudden:** Med. Rec., N. Y., xxvii. 1885, p. 357. **Pye-Smith**

(Traumatic): Trans. Path. Soc. Lond., xxvii. 1876, p. 27. **Ramskill:** Reynolds' Syst. Med., ii. 1868, p. 397. **v. Recklinghausen:** Arch. f. path. Anat., xxx. 1864, p. 374. **Seitz:** Der Hydroceph. Acutus d. Erwachsenen, 1872. **Wilks** (Acute): Guy's Hosp. Rep., vi. 1860, p. 101; *also*, J. Ment. Sc., x. 1864, p. 520. **Williams:** Texas Med. and Surg. Rec., Galveston, i. 1881, p. 312. **Wood:** Arch. Pediat., Phila., i. 1884, p. 748.

250. **Hydrencephalocele and Meningocele.**—It occasionally happens that a congenital local deficiency in the bony case of the cranium exists at some part, and a protrusion of the brain covered by its membranes, or of the membranes alone, takes place through it. In the first case the condition is known as a **Hydrencephalocele,** in the latter as a **Meningocele.** The aperture in the skull is usually round, and most commonly situated at the occiput or at the root of the nose. Whether the bony defect is the *result* or the *cause* of the tumour remains undecided. If the latter, the fact might rank as an argument in favour of the view that the yielding capacity of the cranial vault is the cause of hydrocephalus internus.

Literature of Hydrencephalocele and Meningocele.—**Agnew:** Med. and Surg. Reporter, Phila., xxiii. 1870, p. 32. **Ahlfield:** Die Misshildungen d. Menschen. Ab. ii. 1882. **Baxter:** Trans. Path. Soc. Lond., xxxiii. 1881-2, p. 1. **Breesnee:** Bijdrage tot de kennis der hydromeningocele, 1870. **Marshall:** Lancet, 1885, i. p. 890. **Pepper:** Ann. Journ. M. Sc., Phila., lix. 1870, p. 417. **Ziegler:** Path. Anatomy (transl.), pt. 1, 1883, p. 27.

251. **Hydrorachis.**—This is the generic term employed to indicate a distension of the spinal cord or its membranes by cerebro-spinal fluid. Where there is a universal or widespread distension of the central canal the term **Hydromyelia** (μυελός, marrow) is usually given to the condition, while that of **Syringomyelia** (σῦριγξ, a tube) is more commonly applied to irregularly-shaped cavities found in the substance of the cord either connected with the central canal or not (Langhans, No. 13, lxxxv.) The former is, as a rule, congenital, whereas the latter in most cases seems to be a product of after life.

The designation of **Spina bifida** is given to that condition in which some part of the vertebral arch is deficient, thus allowing the membranes to protrude in a cyst-like tumour. The deficiency in the vertebræ comprises that of the spines and laminæ, and is, in most cases, situated in the lumbar or lumbo-dorsal region. Cases do occur in the cervical part of the spinal column, and, when so, they are usually accompanied by some defect in the bones of the skull. There is commonly only one tumour, but several have been described in the same subject. The tumour forms externally a rounded or somewhat flattened doughy swelling, which increases in size while the patient is in the erect position, but subsides partially or completely when prone.

There is occasionally an umbilicus-like *depression* on the surface, corresponding to a point to which the end of the spinal cord has become adherent. According to Virchow (No. 13, xxvii. p. 576), it is only in cases located at the very lowest point of the spinal canal that the tumour is a pure **Hydromeningocele,** that is to say, in

which the cyst is composed entirely of the dura mater or of this with the dropsical arachnoid. Such cases are rare. In by far the greater number of instances the sac consists of the skin and immediately subcutaneous tissues, together with the membranes covering the cord, and into it the cord has been dragged. In the ordinary lumbar or lumbo-sacral variety the spinal cord is attached by its termination to the depression on the surface.[1]

The *nerves* of the cauda equina or cord are flatly applied to the interior of the sac previous to their being peripherally distributed. In some cases there may be a communication between the sac and the central canal of the spinal cord through a cleft in the latter, so that the liquid of the sac and that of the cerebro-spinal central canal freely intermingle.

Cause.—Here there is the same difficulty as in the case of the Encephalocele, in saying whether the formation of the sac or the deficiency of the vertebræ has been primary. The matter is so uncertain that the author refrains from giving any opinion.

The irregularly shaped or **syringomyelitic cavities** sometimes seen in the spinal cord appear to arise in several ways (Leyden, No. 13, lxviii.; and Langhans, No. 13, lxxxv.) Some of them are mere offshoots from the central canal of the cord, and when so, are usually located in the gray matter; while others may arise from hæmorrhages and softenings of the white matter of the cord from which the débris has been absorbed. The former are lined by cylindrical epithelium, the latter are commonly not.

Literature on Hydrorachis and Spina Bifida.—**Ahlfield:** Die Missbildungen d. Menschen, 1882. **Ashurst:** Syst. Pract. Med. (Pepper), Phila., v. 1886, p. 757. **Barron:** Lancet, 1882, ii. p. 1108. **Demme:** Wien. med. Blatt, vii. 1884, p. 803. **Fürstner and Zacher** (Formation of Cavities in Cord): Arch. f. Psychiat., xiv. 1883, p. 422. **Hofmokol:** Arch. f. Kinderh., iii. 1881-2, p. 112. **Humphry:** Lancet, 1885, i. p. 557; *also*, Journ. Anat. and Physiol. xix. 1884-5, p. 500; *Ibid.*, xx. 1885-6, p. 585. **Jacobi:** Med. Rec. N. Y., xxiii. 1883, p. 357. **Klein:** Zur Casuistik d. Sp. Bifida, 1885. **Maclean:** St. Thomas's Hosp. Rep. (1884), xiv. 1886, p. 247. **Marchand** (Recent Works on S. B.): Deut. med. Wochnschr., viii. 1882, p. 527. **Moore:** Med. Times and Gaz., 1880, ii. p. 522. **Morton:** Brit. Med. Journ., 1883, i. p. 82. **Parker** (Rep. of Committee): Lancet, 1885, i. p. 989; *also*, Brit. Med. Journ., 1885, i. p. 1098. **v. Recklinghausen:** Arch. f. Path. Anat., cv. 1886, p. 296, *et seq.* **Roberts:** N. Y. Med. Journ., xxxix. 1884, p. 89. **Shattock:** St. Thomas's Hosp. Rep. (1884), xiv. 1886, p. 248. **Thomas:** Gaillard's Med. Journ. N. Y., xxxix. 1885, p. 237. **Tourneux and Martin:** Journ. de l'Anat. et. Physiol., xvii. 1881, p. 1. **Westphal** (Syringomyelia, transl.): Brain, vi. 1883, p. 145. **Whithead:** Brit. Med. Journ., 1883, ii. p. 825; *Ibid.*, 1884, i. p. 165.

252. **Hydrocele.**—In an ordinary **hydrocele** the accumulation of liquid takes place in the sac of the tunica vaginalis. The testicle is pushed backwards and flattened, and may ultimately undergo atrophy from the pressure of the liquid.

[1] Morgagni ("De sedibus," quoted by Virchow, *loc. cit.*) was at a loss to know how the cord could be present in a part of the spinal column where only cauda equina naturally exists. Virchow explains it embryologically by the spinal cord extending originally throughout the entire spinal canal.

Congenital Hydrocele is a dropsy of the tunica where in addition the original opening between the peritoneal cavity and the sac remains patent.

The term **encysted hydrocele** is somewhat of a misnomer. The disease is constituted by the dropsical dilatation of tubular structures probably derived from the vas aberrans of the epididymis. They are commonest over the epididymis. The cyst invaginates itself into the tunica vaginalis, but the cavities do not communicate.

Causes.—The principles upon which a hydrocele fluid is thrown out are as yet obscure.

Literature on Hydrocele.—**Agnew**: Hydrocele, 1877. **Alisch**: Zur Aetiologie u. Therap. d. Hyd., 1876. **Béchamp** (Fluid of): Compt. rend. Acad. d. Sc., lxxxvi. 1878, p. 67; *Ibid.*, lxxxviii. 1879, p. 608. **Boursier**: Étude sur les Hyd., 1880. **Bricard**: Des Kystes Spermatiques, 1877. **Chollet**: Rec. sur l'Étiologie de l'Hyd., 1879. **Curling**: Trans. Path. Soc. Lond., ix. 1857, p. 316; *also*, Practical Treatise on Diseases of Testis, etc. 1878. **Deladrière**: Essai sur les Hyd. enkystées, 1879. **Hoppe**: Deut. Klinik., Berl., ii. 1850, p. 481. **Hue**: De l'Hyd. enkystée, 1873. **Marimon**: Rech. sur l'Anat. path. des grosses Hyd., 1874. **Osborn**: Hydrocele, 1878. **Panas**: Arch. gén. d. Méd., 1856, i. p. 670. **Saint-Germain**: N. Dict. de Méd., et Chir., xviii. 1874, p. 1. **Syme**: Lancet, 1855, i. p. 447. **Villegente**: Du Mode de Formation des Kystes Spermatiques, 1874.

253. **Hydronephrosis.**—A dilatation of the ureters and pelvis of the kidney is usually caused by some *impediment to the outflow of urine* from them. Complete obstruction causes, in a short time, a total suppression of urine.

Causes.—The chief are the *impaction of a calculus* in the ureter, and constriction of it by fibrous adhesions, by a cancer of the uterus, or by the two combined. Tumours of the pelvis are also apt to press upon the exit of the ureter, or the obstruction may be lower down in the urethra or prostate. The *ureter* becomes distended and tortuous, a sigmoid bend shortly below the kidney being specially remarkable. In course of time the *calices* and even the *urinary tubules* may become similarly distended, and as a result of the pressure, more or less complete atrophy of the kidney follows. The distending force is the pressure at which the urine is excreted, together with the weight of the column of liquid in the upright position of the body from the kidney down to the point of stricture.

Literature on Hydronephrosis.—**Ange**: De l'Hydronéphrose, 1878. **Bidder**: Berl. klin. Wochnschr., xxii. 1885, p. 118. **Billroth**: Allg. Wien. med. Ztng., xxix. 1884, p. 28. **Broadbent** (Congenital): Trans. Path. Soc. Lond., xvi. 1864-5, p. 165. **Coats**: Glasg. Med. Journ., xix. 1883, p. 73. **Cotter**: Med. Times and Gaz., 1879, ii. p. 184. **Dickinson**: Renal and Urinary Affections, pt. iii. 1885. **Finlayson**: Glasg. Med. Journ., 1874. **Galliard**: Progrès méd., viii. 1880, p. 868. **Heusser**: Ein Beitrag z. Kenntniss d. Hydrn., 1878. **Hortolès**: Trav. du Labor. d'Anat. gén. et d'Histol., Paris, 1882, p. 200. **James**: Edin. Med. Journ., xxiii. 1877-8, p. 135. **Lee**: Med. Rec. N. Y., i. 1866-7, p. 418. **Moreau**: Hydronéphrose, 1868. **Peters**: Med. Rec. N. Y., xxi. 1882, p. 477. **Roberts**: Reynolds' Syst. Med., v. 1879, p. 587. **Rosenstein**: Path. and Ther. d. Nierenkrankheiten, 1863-70. **Simpson**: Hydronephrosis, 1867. **Spencer-Wells**: Med. Times and Gaz. 1868. **Virchow** (Congenital): Verhandl. d. phys. med. Gesell. in Würzb., v. 1855, p. 447; *also* Die krankh. Geschwülste, 1863.

254. **Œdema of the Lung.**—When a lung becomes œdematous it appears to have much increased in size, in fact it may resemble a pneumonic organ when first cut into. On being squeezed, however, the liquid contained within it is readily expressed, leaving the collapsed lung tissue. In pneumonia it is impossible to remove the materials producing the solidification. The liquid appears to be contained both in the interstitial tissue and in the air-vesicles. There is very frequently much congestion along with the œdema.

Causes.—Œdema of the lung is associated with so many diseases that it is impossible to lay down any general law as to its cause. Many œdematous liquids of the lung are considered to be effused *in the agony* and hence are unimportant. In the general anasarca of *renal disease* the lungs usually participate largely, and in *valvular disease* of the heart they are sometimes, but not always, œdematous. The dropsy of the *special cachexiæ* is also a cause.

Experimental Evidence.—The experimental facts seem to be of a somewhat contradictory nature, and as yet have not cleared up the subject. Cohnheim and Lichtheim, in their previously quoted research (No. 13, lxix.) showed that œdema is by no means a constant accompaniment of hydræmic plethora in the dog, brought about by the injection into the circulation of large quantities of salt solution. It might be supposed that an elevation of the pressure within the pulmonary system of vessels might have the effect of inducing an increased transudation of liquid. Welch (No. 13, lxxii.) and Cohnheim (No. 31, i. p. 419) have, however, proved that an elevation of the pressure within the pulmonary artery of very considerable moment is insufficient to induce an œdema of the organ. It is only where the pressure rises far above what could ever be anticipated in Man that any œdema is perceptible.

Even the retardation of the venous outflow by ligature of the pulmonary veins or by stenosis of their orifices, seems to be only very slightly instrumental in causing an œdema (Cohnheim, *loc. cit.*)

Welch (*loc. cit.*) arrived at the conclusion that one of the most effectual means of exciting pulmonary œdema artificially in an animal is by inducing a *left-sided paralysis of the heart.* He brought this about by squeezing it. He asserts, in explanation, that when the left ventricle becomes weakened it is unable to remove the blood which is being pumped into the lung by the right, and theoretically, he states, one may suppose that the pressure rises to a great height within the pulmonary vessels on this account. Although admitting, however, that a left-sided paralysis of the heart may be the proximate cause of acute œdema of the lung, he would not undervalue the influence of *cardiac incompetency, hydræmia*, etc., in predisposing to œdema of the lung. What he would emphasise is that *taken alone* these are insufficient to account for it.

Sahli (No. 104, vol. xix. p. 433) differs in his results from Welch, and affirms that an œdema of the lungs in accord with his theory is never brought about pathologically. Most of the œdematous conditions of the human lung are not obstructive in their nature but are either due to local inflammatory causes or are of the nature of the closely related nephritic or cachectic œdemas.

General Characters of Dropsical Transudates.

255. As a rule they are pale yellow or greenish, limpid liquids with a saltish taste, alkaline reaction, and with a specific gravity ranging from 1005 to 1024. They all contain albumin and throw down a precipitate with heat and nitric acid.

Coagulability.—None of the purely dropsical liquids in Man have the power of coagulating spontaneously.[1] The most of them, nevertheless, contain fibrinogen and fibrino-plastic substance (serum-globulin or paraglobulin). What is evidently wanting in order to induce coagulation is the fibrin ferment. This was formerly supposed to be present for the most part in the colourless corpuscles. It seems probable, however, that the source of it is to be sought in considerable part in the *hæmatoblasts or blood-plates.* These, in dying and disintegrating, shed the ferment which they contain into the surrounding liquid, which then causes the precipitation of the fibrinogen in the form of fibrin. If, as Buchanan (No. 178, 1845, i. p. 617; and Gamgee, No. 179, ii. 1879-80, p. 145) showed, a small piece of blood clot be squeezed in a linen cloth, and if the expressed liquid be added to dropsical effusions of various serous cavities, a fibrinous coagulum is precipitated. The addition of a small piece of the squeezed blood clot or of blood serum to hydrocele fluid has the same effect. In the case of the squeezed blood clot the coagulum is thrown down in its immediate vicinity. The explanation of the phenomenon most probably is that the expressed **liquid** of the clot, the **squeezed clot** itself, and the **blood serum** all contain the fibrin ferment. Into blood serum it is probably copiously shed from the blood-plates as coagulation is taking place.

Composition.—The proteid constituents are very much like those of blood serum, although they never equal them in amount (Runeberg). The quantity of proteid matter, moreover, in a purely dropsical transudation never comes up to that of an inflammatory exudation (Lassar). Certain peculiar substances, probably degeneration products, are found in some dropsical liquids which are not components of the blood.

Béchamp (No. 40, lxxxviii. No. xi. 1879) formerly discovered that the albuminous substances in **hydrocele fluid** possessed the power of **rotating the plane of polarisation** 70° to the left. He asserts that he has been able to isolate different albuminous bodies from this fluid by successive precipitation with lead acetate. He employs firstly a *neutral solution* of acetate of lead, and gets a precipitate with this. From the filtrate he gets a second precipitate with *basic* acetate of lead; and from the filtrate of this a third precipitate with *strong basic* lead solution. The first and third precipitates when separated from the lead with carbonic acid, both show powers of rotation different from the original liquid. They are precipitated by alcohol and

[1] Gamgee (No. 21, p. 44) states that the liquor pericardii of the rabbit coagulates with readiness.

redissolve in water. They differ from the albuminous bodies of the pleural, peritoneal, or pericardial effusions, and from the albumins of blood; and he supposes they become altered in their passage through the wall of the sac.

The proteid matters usually present in dropsical liquids are chiefly serum albumin, fibrinogen, and serum globulin or paraglobulin. The serum albumin is itself soluble in water, the fibrinogen and globulin are held in solution by the aid of sodium chloride. The salts are of the same nature and in the same proportion in all dropsical liquids as in the liquor sanguinis. The extractive matters also bear a like relationship to those of the blood. Gases such as carbonic acid, oxygen, and nitrogen are moreover present.

Certain special products, such as grape sugar, or at least a substance which reduces copper, can be separated from dropsies of particular parts (see Turner, No. 149, vii. 1854; Rosenbach, No. 180, No. 5, 1852; No. 49, vol. i. p. 255, 1882; and Hoppe-Seyler, No. 30, p. 326). Eichorst (No. 91, 1881, p. 537) discovered sugar or a sugar forming substance in seventeen pleural effusions. In one case the substance was glycogen. He states that of seventeen exudates he found ten containing grape sugar, two free from sugar and containing a diastatic ferment, and five containing sugar but ferment free.

Metalbumin (Scherer, No. 20, lxxxii. p. 135) is a proteid substance found in ascitic fluid, which gives certain reactions different from serum albumin.[1]

Paralbumin is found in ovarian cysts and gives to the contents the peculiarly ropy character which they often possess.[2]

Casein and *myosin* are occasionally met with in small quantity. Dropsical liquids of joints usually contain some *mucin*. *Hæmoglobin* and other colouring substances may be present in certain of them. They often contain quantities of desquamated *endo- or epithelium*.

256. **Hydrops Lacteus.**—Occasionally the dropsical liquid of the abdominal cavity or that of the pleura presents a milky opacity. In some instances it exactly resembles milk of poor quality. Numerous cases of this disease have been recorded from time to time. The best described are perhaps those of Guttmann (No. 43, No. xxix. 1880), Stern (No. 13, lxxxi. p. 384, 1880), and Whitla (No. 6, May 30, 1885), the last with a chemical analysis by Hay.[3]

Microscopically examined the liquid is found to contain numerous oil globules, lymph cells, and crystals. In Whitla's case Hay found on analysis that the liquid had a specific gravity of 1014, it did not coagulate spontaneously, but did so with heat and nitric acid. It had an alkaline reaction and contained

[1] Not precipitated by acetic or hydrochloric acid; on boiling gives a slight cloudiness, but no flocculent precipitate on subsequent addition of acetic acid.

[2] Soluble in water on account of its alkali; precipitated by alcohol; redissolved in warm water.

[3] Consult also Cohnheim (No. 31, i. p. 406), Dreyfus-Brissac (No. 181, September 9, 1882), Perrée (No. 182), and Quincke (No. 140, xvi. 1885).

Water . .	94·085.	Inorganic matter . .	0·995.
Solids . .	5·915.	Organic . . .	4·920.
		Albumin . . .	2·878.
		Fat	1·030.
		Sugar . . .	0·210.
		Other organic materials	0·802.

The liquid appeared to be formed of almost pure chyle.

The usual **pathology** of these cases consists in a **lymph fistula** having been established through rupture of some part of the thoracic duct or receptaculum chyli. In the above case an opening was found in the receptaculum capable of admitting a No. 2 catheter. The cause of the rupture is usually the obstruction caused by pressure of a tumour upon some part of the duct. Ludwig and Cohnheim have shown that ligature of the thoracic duct causes the peripheral part to become varicosely dilated, a condition which is followed in course of time by rupture of the receptaculum. A permanent lymph fistula is subsequently established.

Literature on Hydrops Lacteus.—**Ballmann:** Centralbl. f. d. med. Wissensch., xiv. 1876, p. 275. **Bergeret:** Journ. de l'Anat. et. d. l. Physiol., ix. 1873, p. 586. **van Camp:** Ann. Soc. de Méd. d'Anvers, iii. 1842, p. 86. **Duffey:** Brit. Med. Journ., i. 1886, p. 71. **Hughes and Rees:** Guy's Hosp. Rep., vi. 1841, p. 297. **Letulle:** Rev. de Méd., v. 1885, p. 960. **Lorain:** Compt. rend. Soc. de Biol., v. 1859, p. 162. **Martin:** Journ. de Méd. Chir. Phar., etc., xxxiv. 1770, p. 555. **Milleret:** Journ. de Méd. Chir. Phar., etc., xliii. 1774, p. 231. **Popham:** Dub. Quart. Journ. Mic. Sc., xvii. 1854, p. 467. **Quincke:** Deut. Archiv. f. klin. Med., xvi. 1875, p. 121. **Stevenson:** Guy's Hosp. Rep., xvii. 1872, p. 231. **Straus:** Arch. de Physiol. norm. et path., vii. 1886, p. 367. **Veil:** Étude sur la Pathogénie des Ascites clyliformes, 1882. **Weaver:** Lond. Med. Repositor, ii. 1814, p. 377. **Wilks and Ormerod:** Trans. Path. Soc. Lond., xix. 1868, p. 199. **Winckel:** Deut. Arch. f. klin. Med., xvii. 1876, p. 303.

Products of Decomposition of Dropsical Liquids.—Dropsical liquids, especially if at any time they should become purulent, occasionally contain certain products of decomposition. *Leucin*, *tyrosin*, *xanthin*, and *cholesterine* are among the commonest.

Literature on General Characters of Dropsical Transudates.—**Becquerel and Rodier:** Chimie Path., 1854. **Bock** (Sugar in): Arch. f. Anat. Phys., etc. 1873, p. 620. **Cheyron:** Des Liquides Ascitiques, 1879. **Garré:** Cor.-Bl. f. schweiz. Aerzte. xvi. 1886, p. 473. **Hammarsten** (Metalbumin and Paralbumin): Zeitschr. f. physiol. Chem., vi. 1882, p. 194. **Hoppe:** Deut. Klinik, 1853. **Klemensiewicz:** Mitth. d. Ver. d. Aerzte in Steiermark, xxi. 1885, p. 114. **Lehmann:** Lehrbuch d. phys. Chemie, 1853. **Schmidt:** Arch. f. Anat. Physiol., etc. 1861, pp. 545, 675; 1862, pp. 428, 533. **Tidy** (in Hydrocephalus): Lancet, 1869, i. p. 156.

Amount of Proteids in various Dropsies.

257. The amount of albumin found in dropsical liquids varies in different cases, when taken from the same cavity, or in any one instance of general dropsy, when taken from different cavities. The *relative* quantity found in the cavities of the body, however, unless under very exceptional circumstances, remains pretty constant. Thus,

it is generally greatest in the **pleural cavity**, next in the **abdomen**, next in the **cerebral ventricles**, and least in the **subcutaneous areolar tissue**.

Schmidt (No. 183, p. 146) found that in 1000 grammes transudation the albumin contained in the various cavities stood in the following quantitative relationship :—

Pleura	Peritoneum	Cerebral ventricles	Subcutaneous
28·5	11·3	8·0	3·6

Hoppe-Seyler (No. 13, ix.), in an instance of general anasarca from Bright's Disease complicated by catarrh of the bladder, gives the total solids in 1000 parts transudation as :—

Pleura	Peritoneum	Subcutaneous
42·41	32·32	17·83

the quantity of salts remaining constant.

Lehmann (No. 184, ii. p. 316) made out the proportion of albumin in a drunkard with cirrhosed liver to be

Pleura	Peritoneum	Cerebral ventricles
18·52	10·44	5·64

The only feasible explanation of this fact has been given by James, from whose paper on "Transudations and Exudations" (No. 185, 1889) the above figures have been quoted. He asserts, with very good show of reason, that the negative pressure of the pleural cavity will, *ceteris paribus*, tend to *aspirate* a liquid richer in albumin than would be effused into a part where such does not exist. The movements of respiration will have a like effect in the abdomen but to a less degree. The effusion into the pericardium is sometimes highly loaded with proteids, probably from the aspiration caused by the movements of the heart (consult Brunton, No. 173, p. 336).

The effused liquids, however, also tend to become *concentrated* as the effusion accumulates from absorption of the water. When this occurs the pressure will be found to be *positive* (Hoppe-Seyler, No. 13, ix. p. 245, 1856). Thus Quincke (No. 140, xxi. p. 453, 1878) found that the pressure of ascitic liquids measured through a puncture of the abdomen immediately above the symphysis pubis in the upright position of the body fluctuated between + 26 to + 58 cm. of the transuded liquid, and that the respiratory movements made a difference of about 2 to 3 cm. In the pleura distended with liquid he found on an average that it was equivalent to + 10 mm. Hg. This positive result would naturally ensue when the accumulation of the liquid had taken place to such an extent as to compress the lung and destroy its elastic pull upon the pleural cavity. When the liquid is withdrawn, the intra-pleural pressure again becomes negative.

Leyden (No. 22, iii. p. 264, 1878) says that in a number of cases of pleurisy and empyema the pressure of the exudate at the time

of puncture read 0, + 1, to + 28 mm. Hg; while, after the removal of the effusion, the pressure in the pleural cavity sank to − 2, − 28, to − 42 mm. Hg. In only one case was the pressure ultimately + 4. The movements of respiration made a difference of 1 to 20 mm.

Forced *expiratory efforts* as in coughing will probably tend to concentrate such liquids.

Bochefontaine (No. 40, lxxxvi. No. 25, 1878) found, on the contrary, that the pressure in health of the **cerebro-spinal liquid** in chloralised animals, when they are lying quietly and breathing easily, was just equivalent to that of the atmosphere, and that each systole of the heart made a difference of + 0·5 mm. Hg. Under the influence of forced expiratory movements it may rise to + 5·5 mm.

258. **Quantity of Proteids and Diagnosis.**—The quantity of proteids in ascitic liquid forms an important aid to diagnosis. Runeberg (No. 140, xxxiv. p. 1, 1883), from the examination of a large number of pathological transudates, has arrived at the following definite conclusions :—(1) 0·3 per cent albumin and below this always means a hydræmic ascites. (2) 0·3 to 0·5 per cent, also a hydræmic ascites but where the hydræmia is less pronounced; or a transudate with commencing absorption; or portal stasis with great hydræmia; or ordinary stasis with very great hydræmia. (3) 1·5 per cent indicates portal stasis, or ordinary venous stasis with great hydræmia. (4) 1·5 to 2 per cent is generally due to ordinary venous stasis, portal stasis where the body is well nourished, an old transudate, or a transudate with commencing absorption. (5) 2 to 2·5 per cent means ordinary venous stasis in a well nourished subject; portal stasis exceptionally in old people; a transudate under high tension; or a transudate in process of absorption. (6) 2·5 to 3 per cent indicates a transudate due to carcinoma or inflammation where there is a very great amount of cachexia. (7) 3 to 4·5 per cent, a carcinomatous or inflammatory transudate with ordinary cachexia. (8) 4·5 to 6 per cent, a peritonitis in a well-nourished individual; in exceptional cases an old transudate from a carcinomatous peritonitis; and where there is much compression from stretching of the abdominal wall.

Hoffmann (No. 49, p. 239, 1881) divides ascitic liquids into three classes according to the quantity of albumin they contain :—(1) **Cachectic** ascites, specially where due to chronic renal disease, and where the albumin is below 1 per cent and the specific gravity under 1010. (2) **Inflammatory,** where the albumin is over 2·5 per cent and the specific gravity over 1014. (3) **Congestive,** lying between these.

259. **Quantitative Analysis of Proteids.**—A very close approximate, quite sufficiently accurate for most purposes, of the percentage amount of albumin in dropsical liquids may be obtained by Reuss' formula (No. 140, xxviii. p. 317, 1881). Let A be percentage amount of albumin and S the specific gravity of the liquid. Then

$$A = \frac{3}{8}(S - 1000) - 2{\cdot}8.$$

There are variations $\pm \frac{1}{4}$ per cent which are unavoidable.

Runeberg (No. 140, xxxv. p. 266, 1884) on the same calculation as that of Reuss recommends the formula

$$A = \tfrac{3}{8}\,(S - 1000) - 2{\cdot}73$$

for dropsical effusions, and

$$A = \tfrac{3}{8}\,(S - 1000) - 2{\cdot}88.$$

for those which are of inflammatory origin. The solids are always somewhat greater in transudates when removed from the dead body than from the living.

Esbach's Tubes.[1]—Another means of estimating the quantity of albumin in a liquid is by means of what are known by the above title (see description by Veale, No. 6, i. p. 898, 1884). They are generally employed for albuminous urine, and give very accurate results.

The method consists in observing, in a graduated tube, the height of the deposit given by a measured quantity of albuminous liquid, when treated with picric and citric acids in solution in the proportion respectively of 1 and 2 per cent. The tube is graduated in such a manner that each degree of the deposit corresponds to a gramme of dry albumin per thousand of liquid.

FEVER.

(See Vol. ii., "Vegetable Parasites.")

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[1] These tubes can be had from Messrs. Townson and Mercer, 89 Bishopsgate Street, London, E.C.

PART III

DISEASES OF THE VARIOUS TISSUES AND ORGANS

CHAPTER XXIII

THE STRUCTURE OF CELLS AND THEIR REPRODUCTION

260. **Definition of term "Cell."**—The original definition of a cell, according to the Schleiden and Schwann idea, was a body made up of a cell membrane, cell contents, nucleus, and usually, a nucleolus. In such a sense, the term was apposite; that is to say, it signified a hollow body with a distinct wall and certain contents.

It has been shown, however, that many animal cells are not possessed of all these constituents. A limiting membrane is just as often absent as present, and it is doubtful whether a nucleolus can be looked upon as of constant occurrence. All that the term *cell* in its general acceptation means at the present day is *a nucleated mass of protoplasm.*

Flemming (No. 86, p. 72) defines a cell thus:—

(1) *A mass of circumscribed living substance with or without a special formed membrane.*

(2) *In its interior a cell nucleus,* i.e., *a circumscribed body having a special chemical constitution.*[1]

(3) *With property of forming new compounds out of those substances taken into it.*

(4) *Capable of increasing by division.*

(5) *With a peculiar construction of its substance and of that of the nucleus whereby both essentially consist of threads and intermediate substance.*

It is extremely questionable whether any cell can exist in a living condition without a nucleus. Some years since there was an inclination among histologists to disparage the importance of the nucleus. The discoveries of later times, however, have shown it to be the most important part of the cell so far as the vitality and regeneration of the latter are concerned.

STRUCTURE OF CELLS.

261. The structure of the various parts of the animal cell according to Flemming (*loc. cit.*) is the following:—

[1] Contains nuclein.

The cell body is made up of two substances, of which the one is disposed in threads, and the other is homogeneous.

To the former he gives the name *mitoma* or *cyto-mitoma* (μίτος, thread), and to the other *paramitoma*, or the *filar* and *interfilar* substances.

Kupffer (No. 87, i. 1875) named these two substances respectively *proto-plasma* and *paraplasma*. The word *protoplasm*, has, however, such an ambiguous meaning at the present day that Flemming proposes to do away with it altogether, substituting that of *cell substance* or *cell body* for what in times gone by has usually been designated by this term.

The *cyto-mitoma*, or thread-like basis of the cell body, Flemming asserts, is seldom distributed in the form of a network. Klein and Heitzmann have represented it as such; but a complete equal-meshed network, as that, for instance, which the former has figured in liver cells (No. 88), Flemming believes can only have been artificially produced by the action of reagents. Spirit sometimes causes a vacuolar appearance, which might be mistaken for such a network. The occurrence of particles of secretion within the cell body in those cells engaged in performing some secretory function, such as chalice cells or the epithelium of mucous glands, can also break up the continuity of the cell body in such a manner as to simulate a network. Even in cartilage cells, where it is very well developed, it seldom forms more than a *series of irregularly twisted threads.*

The nucleus is composed—(1) Of **a nuclear network** or *karyo-mitoma* (κάρυον, nucleus), consisting of threads, whose arrangement is such that they form a much more regular net-like figure than those in the cell body. It stains with logwood, safranin, etc., and hence is sometimes called the *chromatin*. (2) **Nuclear sap**, or the substance contained in the meshes of the former. It does not stain with the foregoing reagents, and hence is named the *achromatin* (Flemming). (3) **A nuclear membrane** made up of two layers; an outer which does not stain (achromatic), and an inner, which does (chromatic).

The nucleoli are constructed of a substance more refractile than either the network or nuclear sap. They have a smooth rounded surface, are mostly suspended in the network, but are sometimes intercalated between its fibres. A great many nucleoli, or bodies described as such, are simply coils of the network seen on optical section. The true nucleoli are usually multiple.

REPRODUCTION OF CELLS.

262. It is generally admitted that cells, in the act of reproduction, divide in two ways, either *indirectly* or *directly*. By the former is meant a process by which the network within the nucleus undergoes great development, and is subject to certain transformations of form, which, it is supposed by most histologists, are instrumental in bringing about its division and that of the cell body. This process is usually termed *karyokinesis*

(κίνησις movement), or *karyomitosis* (Flemming). By the latter is understood a means of cell proliferation, whereby the nucleus and cell divide without this growth of the intranuclear network taking place. Many cells, which were said to divide by this latter method, have, however, of late been proved in reality to reproduce themselves by *karyomitosis*.

A. Indirect Method.

263. The following, according to Flemming (*loc. cit.*), are the phases passed through in the indirect division of the nuclei of animal cells, and Strasburger (No. 89) has shown that, with slight modifications, the same cycle of transformations is followed in those of plants.

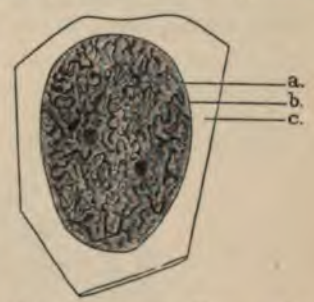

Fig. 110.—Resting Nucleus: Epithelial Cell of Salamander entering upon the "Glomerular" Phase (Flemming).

(*a*) Poorly developed coils of nuclear network; (*b*) nuclear membrane; (*c*) cell body.

Resting Nucleus.—During the time that the cell is not actively engaged in division, the thread network in the nucleus (*resting nucleus*) is meagrely developed. A few coils of a thread here and there are usually all that is to be seen.

Phase I.—*Commencement of division; Formation of the poles; Nuclear glomerulus figure.*

The first sign of division being about to take place, according to Flemming (*loc. cit.* p. 199), is the formation within the cell-body of two poles opposite each other and close to the circumference of the nucleus. These poles can be recognised in the living cell by the accidental presence of granules or of pigment particles, which become radially aggregated into two groups, with a clear space (Arnold) or pole in the centre of each.

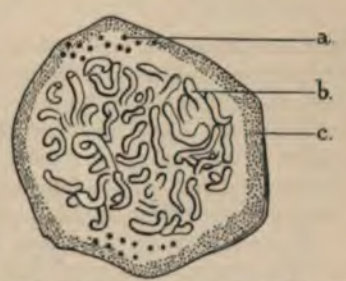

Fig. 111.—Phase I. Living Cell of Salamander (Flemming).

(*a*) Granules aggregated round a pole of the cell; (*b*) coils of "glomerular" network; (*c*) cell body.

The next thing noticed is that the few coils seen in the threadwork of the resting nucleus become much more evident. The threads become thicker and more numerous and tortuous. This increase in the network is brought about evidently by a longitudinal segmentation or splitting of its threads, and when complete, the stage is called by Flemming the *total or complete form* of the resting nucleus.

The outer or achromatic layer of the nuclear membrane, now that the process of nuclear division has commenced, becomes more evident than it was round the resting nucleus; it appears to have increased in thickness.

Phase II.—*Star form (aster) of the nuclear network together with the transformation of the glomerulus into the same.*

Two sets of phenomena are seen in this, namely (1) those of the chromatic nuclear network, and (2) those of the achromatic part of the nucleus.

(1) **The Chromatic Figure.**—In most cells (epithelium, connective tissue, muscle, nerve, and different glands) the nuclear membrane now

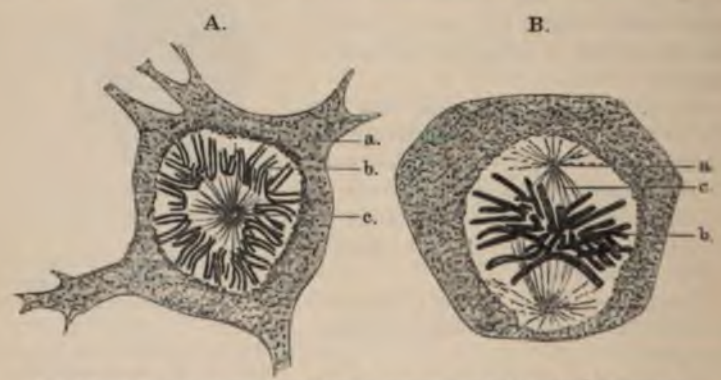

FIG. 112.—PHASE II. ENDOTHELIAL CELLS, ABDOMEN OF SALAMANDER (Flemming).

A, Surface view of nuclear network: (a) cell body; (b) threads of network; (c) one of the poles with the achromatic threads radiating from it. B, Equatorial view of a corresponding cell: (a) one of the poles; (b) the nuclear network seen on edge; (c) the achromatic threads forming a spindle between the two poles.

becomes indistinct, and contemporaneously with, or shortly after this, the segments of nuclear threads which, up till now, have preserved an irregular arrangement, become drawn out into loops with particularly long limbs. These are placed radially with the loop towards the centre of the nucleus, and thus a somewhat star-shaped figure results. In the epidermis of the salamander, Flemming has counted as many as twenty-four of these loops.

It sometimes happens that the conversion of the network into the radially arranged loops of the *aster* does not happen simultaneously. The peripheral as well as the central bends of the pieces of nuclear thread may consequently be seen; and in such a case a figure which he formerly called the *wreath* results.

In the middle of the *aster* is seen a clear space (Fig. 112 A). This always corresponds to the *polar* or diagonal view of the *achromatic spindle*, that is to say, to the part of the nucleus which does not stain.

If one does not find the clear centre, then the star is being looked at on edge, and the achromatic poles will be seen on either side (Fig. 112 B).

(2) **The Achromatic Figure** (Nuclear Spindle).—In animal cells, the chromatic figure always predominates over the achromatic, and hence is apt to conceal it. In plants (Strasburger) the reverse holds good, and consequently, the nuclear spindle is more evident in the latter. There is no doubt, however (Flemming), that it forms a regular part of the process of nuclear division in animal cells. It is occasionally well brought into view by the use of Flemming's osmic acid mixture (see Sect. 268). The achromatic or *nuclear spindle* figure as Bütschli and Strasburger have made known, consists of a bundle of fine colourless fibres which are not, or are only slightly, capable of being stained with certain special nucleus-staining reagents; which are, on the other hand, more or less coloured by hæmatoxylene and various preparations of carmine; which disappear in pepsin solution; and whose

FIG. 113.—PHASE III. EPITHELIAL CELL OF SALAMANDER (Flemming).
(*a*) Pole and achromatic threads; (*b*) cell body; (*c*) disc-like arrangement of chromatic threads at equator of nucleus.

outlines are rendered sharper by hydrochloric and other acids. The chromatic figures are uninfluenced by the last reagents. It is, therefore, to be presumed that the achromatic threads do not contain *nuclein*, while this substance is a main constituent of the chromatic.

Its Origin.—During the time that the *glomerulus* is forming fibres are found between its deeply-stained coils which are very much paler and much less distinct, and one view in regard to the origin of the achromatic spindle is that it is constructed out of these. Another view is that they are first located in and evolved out of the cell substance, and afterwards grow from this into the nucleus. The latter view is probably the more likely of the two, although there are certain facts which are opposed to it.

Phase III.—*Equatorial disc; concentric arrangement of the chromatic figure.*

The loops having formed the *aster*, divide into two groups with

their angles to the poles and their limbs arranged partly obliquely partly perpendicularly to the nuclear equator. A disc-like object is thus constructed, sometimes more or less *barrel shaped*, at other times flat towards the centre of the transformed nucleus, known as the *equatorial disc*. The number of the threads seems to increase in this stage, but they become thinner than in that of the *aster*.

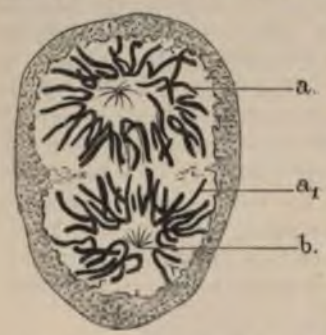

FIG. 114. — PHASE IV. EPITHELIAL CELL OF SALAMANDER (Flemming).

(*a*, *a*) Chromatic threads of daughter asters; (*b*) achromatic threads and pole.

Phase IV. — *Star form of the daughter nuclei* (Dyaster).

This stage comprises that state of the chromatic network in which a separation has taken place at the equator, and in which the divisions of the network become retracted and concentrated round about the poles. The number of the loops is as great as in the mother nucleus in which the threads have not as yet undergone longitudinal splitting. It may therefore be conjectured that the halves of each thread separate into the two daughter *stars*. The threads evidently contract in the daughter network, as their entire volume decreases. There is always a clear point (pole) in the centre of each.

Phase V.—*Glomerular form of daughter nucleus.*

Towards the end of the *dyaster* phase the threads become more convoluted. At first the general direction of these is radial, but soon the type becomes more *wreath like*, and Flemming formerly called this stage the *wreath form of the daughter nucleus*. The network contracts more and more, however, and in time assumes so dense an appearance that the individual convolutions can hardly be recognised. A nuclear membrane also again shows itself. Subsequently to this the network returns to its resting state.

Division of the Cell Body and Termination of the Achromatic Thread Figures.—The division of the cell body, Flemming says, commences with the appearance of the *daughter glomeruli* or towards the end of the *daughter star phase*. The separation of the nucleus thus precedes that of the cell body. The first evidence of it is a constriction of the cell substance at the equator. Sometimes the division is not equilateral, and sometimes the constriction is deeper at one side than at another. A clear refractile girdle forms at the point of constriction. The achromatic threads behave differently in vegetable and in animal cells during the later stages of karyomitosis. In vegetable cells the middle part of the achromatic figure is very evident, and a distinct *equatorial-cell-lamina* in the *daughter star* phase is noticed. This, however, appears to be much less evident, if it is present at all, in animal cells. In the next or *daughter glomerulus* stage, however, the

achromatic threads become very distinct, running between and joining the two new glomeruli, and constricted opposite the indentation in the dividing cell body (Fig. 115). Finally a complete separation follows in the cell body, and consequently in the achromatic threads, and the division of the entire cell is thus completed.

Function of the Karyomitoma.—Although the idea prevalent at the present day is that karyomitosis is the means by which the nucleus is drawn asunder and divided, it should be mentioned that this has been called in question by some histologists. Thus Brass (No. 99,

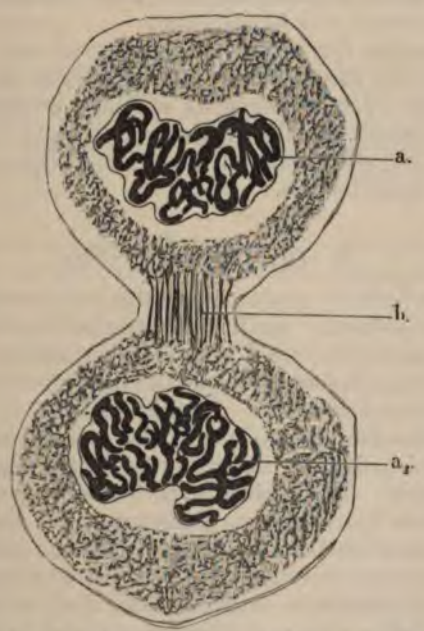

FIG. 115.—PHASE V. EPITHELIAL CELL OF SALAMANDER (Flemming).
(a, a_1) Daughter glomeruli; (b) achromatic threads still uniting the two daughter cells.

vi. Jahrg., No. clvi. 1883, p. 681) makes out from the study of infusoria that the chromatin is merely a result of over-nutrition—a reserve store of nutritive pabulum. It is gradually absorbed during long-continued starvation.

264. **The Indirect Method in Pathological Cells.**—The earlier observations on indirect division were almost all conducted on cells of normal tissues. It has lately been found that pathological cells frequently divide in the same way. The best objects to see it in are perhaps flat-celled epitheliomata. Thus Arnold (No. 13, xli. p. 178) and Martin (No. 13, lxxxvi. p. 56) found it in an actively growing cancer of the mamma and in sarcomata, while Pfitzner (No. 13,

ciii. p. 275) has observed it abundantly in the epithelium a short distance from the edge of healing wounds. Martin's observations have also been confirmed in carcinomata and sarcomata by Aoyama (No. 13, cvi. p. 568). From personal experience, the author can specially recommend flat-celled epitheliomata and the epithelial cells of venereal warts and condylomata, as well as large spindle-cell sarcomata as objects of study. It is a curious fact referred to by Flemming that the karyomitotic figures seem to prevail in certain areas of such tumours. It will often be found that a whole series of sections may be examined without alighting upon any, and suddenly in one or two adjacent sections they may be abundant.

265. **Pluripolar Division.**—In pathological cells, Arnold (*loc. cit.*) and Martin (*loc. cit.*) have noticed that the nucleus and cell body may divide into three or more segments evidently corresponding with so many poles in the cell. Such forms are seldom found in normal tissues.

Cornil (No. 40, ciii., 1886, pp. 78-80) has observed tripolar division in cells of epitheliomata.

B. The Direct Method.

266. It was formerly supposed that this was one of the commonest methods of cell division. As Remak described it, the division commenced in the nucleolus, spread to the nucleus, and ultimately affected the cell body; but, as before remarked, this direct method is evidently of comparatively rare occurrence. Pfitzner (No. 13, ciii. p. 275), lays down the rule that the younger the animal, and the more actively the division of cells is going on, the greater is the frequency of this direct method of division. The nucleus in such cases is poor in chromatin. Thus karyomitotic figures are less abundant in the tissues of the very young embryo than later on; and they are less abundant in the epithelium at the immediate edge of a wound than at a little distance from it.

Division of Nucleus without the Cell.—Arnold (No. 13, xciii.) has described in giant and other cells a direct *fragmentary* division of the nucleus, by which it may split into many parts without contemporaneous division of the cell body. These researches have been in great part confirmed by Werner (No. 13, cvi. p. 354).

Literature on Reproduction of Cells.—**Altmann:** Studien, üb. die Zelle, 1886. **Arnold:** Arch. f. path. Anat. xcviii. 1884, p. 501. **Babes** (Method of Staining): Arch. f. mik. Anat., xxii. 1883, p. 356. **van Bambeke:** État actuel de nos Connaissances sur la Structure du Noyau cellulaire, 1885. **Bonnet:** München med. Wochnschr., xxxiii. 1886, p. 387. **Brass:** Chromatin, Zellsubstanz, u. Kern., 1885. **Bütschli:** Morph. Jahrb., xi. 1885, p. 229. **Carnoy, Gilson, Denys:** La Cellule, 1886. **Courchet:** Du Noyau dans les Cellules végét. et animal., 1884. **Degagny:** Compt. rend. Soc. de Biol., iii. 1886, p. 343. **Frenzel:** Arch. f. mik. Anat., xxvi. 1886, p. 73. **Gillis:** Proliferation de la Cellule par Karyokinèse, 1886. **Hertwig:** Untersuch. üb. Morphol. u. Physiol. d. Zelle., 1884. **Jaworowski:** Archiv. slaves de Biol., Paris, i. 1886, p. 641. **List:** Die Rudimentzellentheorie, etc., 1886. **Platner:** Arch. f. mik. Anat., xxvi. 1885, p. 343. **Rabl:** Morph. Jahrb., x. 1884-5, p. 214. **Thouvenin:** Du Noyau dans les Cellules végét. et animal., 1884. **Unnucleated Cells**—Journ. Sc., Lond., vii. 1885, p. 249.

PRICKLE CELLS.

267. In normal stratified epithelium and much more evidently in that covering morbid growths such as warts, condylomata, and cancers, the edge of the cells frequently presents a number of serrations or teeth, hence the names denticulate or prickle cells ("cellules dentelées"). It was formerly supposed that the serrations of the one dovetailed with those of another. That cannot be so, however, as the prickles of one cell are in apposition with those in the neighbourhood by their apices.

Delépine (No. 5, xviii. p. 442) gives quite a different explanation of them. He finds that they are true fibres which spring from the nucleus of one cell and pass over to that of another. From the fact that they do not stain, as well as for other reasons, he thinks it most likely that they are *part of the achromatic nuclear figure* and that they correspond to the fibres which unite the daughter asters before division of the cell body is completed.

268. **Methods.**—Indirect division may be observed in living tissues such as those of the larvæ of various animals (salamander), and in the epithelium of the tail fin of fishes.[1]

Fixing.—It can be far more beautifully followed, however, in preparations which are fixed by means of some hardening reagent. The karyomitotic figures change very rapidly after death, and hence the tissue must be placed in the fixing liquid immediately after being removed. As the object is to get the reagent to penetrate as rapidly as possible, the pieces of tissue should be in the form of thin slices.

Spirit and the chrome salts are not suitable for this purpose; picric and chromic acids are much more serviceable. The former may be used as a cold saturated solution or more dilute; the latter of the strength of $\frac{1}{10}$ to $\frac{1}{2}$ per cent. Flesch (No. 14, xvi. p. 300) recommends a mixture of chromic and osmic acids. Flemming has used this freely, but states that the nuclear plexus stains much better if a little acetic or formic acid be added to the mixture. The formula he employs is the following:—

Chromic acid .	0·25 per cent	in H_2O
Osmic acid . .	0·1 „	
Acetic acid . .	0·1 „	

This is specially suitable for demonstrating the chromatic plexus of the nucleus. For fixing the achromatic fibres, he says the following mixture is more suitable:—

Chromic acid	0·2 – 0·25 per cent	in H_2O
Acetic acid	0·1 „	

followed by staining in hæmatoxylene.

[1] Consult Flemming (No. 14, xiii. p. 693), Peremeschko (No. 14, xvi. p. 437; and *idem*, xvii. p. 168).

Staining and Mounting.—The staining of the chromatic part of the nucleus can be effected by various nuclein staining reagents. Hæmatoxylene is not always a pure nuclein staining substance. It also colours the achromatic filaments faintly, and hence is justly held to be an extremely useful means of demonstration. Flemming employs a very dilute solution which has stood for a long time, and which will stain the anisotropic parts of muscular fibre. The tissue to be stained should be left in it for from twelve to twenty-four hours.

For demonstration of the nuclear network he recommends above all other methods that of staining by the Böttcher-Hermann process as modified by himself (No. 14, xix. p. 317). To effect this, several staining reagents may be utilised; of all these, safranin is the best, but Magdala red or rose of naphthaline, dahlia, gentian violet, mauve, or mauvine, and several others he enumerates, are almost equally good. The section, after being washed in distilled water, is placed in a mixture of equal parts of saturated alcoholic solution of safranin and water. If dahlia is selected, it is better to dissolve it simply in water, or in water acidulated with acetic acid, instead of in alcohol. The section is allowed to remain in the staining mixture for twelve to twenty-four hours. It is subsequently washed in successive relays of alcohol until it ceases to give off colour, when it will be found that the nuclei have retained the colour, while it has been washed out from other parts. The section should be clarified in oil of cloves or turpentine and mounted in dammar lac. Gentian violet, he says, when employed for chromic acid preparations, gives even sharper figures than safranin. If the preparation tends to shrink when being clarified with oil of cloves, Flemming recommends the use of a mixture of equal parts alcohol and turpentine, followed by pure turpentine instead of the above.

CHAPTER XXIV

THE NEW FORMATIONS AND TUMOURS

269. **Definition of a New Formation.**—*The excessive production of some tissue naturally existing in the body during fœtal or adult life, either locally where such tissue is normally present, or in some part of which it is not an actual constituent.*

They are the group of pathological formations known as the *neoplasmata* (νέος new, and πλάσμα, anything formed or moulded).

The word *tumour* signifies merely a swelling, and is usually applied to a local circumscribed projection. A *neoplasm* generally forms a *tumour*, but a *tumour* is not always due to a *neoplasm*. An abscess, for instance, or a cyst may constitute a tumour, but neither of these is a neoplasm. Some *neoplasmata* do not cause any swelling.

For purposes of description it will, however, be more convenient to describe the *neoplasms and tumours* together.

MESOBLASTIC TUMOURS.—Group I.

THE SARCOMATA (σάρξ, *flesh*).

270. The term *sarcoma* had until comparatively recent times a very misty and uncertain signification, and comprised a number of neoplasms of dissimilar nature. It was applied to any new formation which had a flesh-like consistence,—that is to say, which had the consistence of fresh muscle. At the present day, however, it is limited to a class of tumours having certain specific characters.

Definition.—*A sarcoma is a tumour composed of an embryonic connective tissue which shows no inclination to fulfil its ultimate developmental intention.*

A tumour composed of a fully developed connective tissue, such as the white fibrous, is not a sarcoma, nor is a young cicatrix a sarcoma because the cells in both of these have the inherent property of proceeding to their ultimate stage of development, namely, fibrous tissue. In

the sarcoma, the cells have not this tendency, but remain in their embryonic state, and continue to be reproduced over and over again in this state.

Varieties.—The commonest types are those which are composed of round cells, or spindle-cells, or those in which giant cells are found combined with a spindle-cell matrix. There are many varieties and modifications of these, which will be described in due course.

271. **Sites.**—It may, generally speaking, be said that a sarcoma can grow *in any situation in which connective tissue is present*, and as the epithelial surfaces are practically alone exempt from some sort of connective tissue, they may be held as the only exception to the rule that sarcomata may occur in any part of the body. They are more common, however, in parts where connective fibrous tissue is abundant, such as in the subcutaneous fat, the derma of the skin, periosteum, etc.

272. **Embryonic Significance.**—They are all new growths of some tissue evolved from the *mesoblast*, while the cancerous tumours originate from a derivative of the *epi*, or *hypoblast*.

273. **Malignancy.**—All the sarcomata are malignant—that is to say, they tend to recur locally when removed, or they form secondary tumours in distant organs. The round-cell types are very malignant, especially when pigmented, and are apt to form secondary tumours; while the spindle-cell varieties are characterised by a malignancy which is chiefly local. The name "recurrent fibroid" is sometimes applied clinically to a spindle-cell sarcoma, on account of its tendency to reproduce itself locally when excised.

274. **Signs of Malignancy in Sarcomata and in other Tumours.**—It has just been stated that the sarcomata are all malignant tumours, but the characters by which the malignancy of a tumour can be prognosed have not been described. The following are the chief signs of malignancy in any tumour, *be it sarcoma or cancer*:—

(1) *Size of the Cell.*—As a rule it may be said that the smaller the cells of a tumour the more malignant will it probably be. Thus the small round-cell sarcoma is a more malignant tumour than that composed of giant cells, and the small epithelial cells of a scirrhous cancer of the mamma give rise to a more malignant growth than the large flat epithelial cells of the skin or of a mucous membrane.

(2) *The Number of the Cells.*—If a tumour be purely cellular, the greater is the likelihood of its recurring.

(3) *Activity of the Cells.*—One of the chief diagnostic features of a malignant tumour is the tendency which its nuclei and cells have to divide.

(4) *Shape of the Cell.*—A small round cell, like a lymph corpuscle, will be more readily transported by a blood-vessel or lymphatic than one which is long and tapering; and hence the former will tend to reproduce the tumour in neighbouring parts in preference to the latter. The round cell sarcoma forms secondary tumours in neighbouring organs with greater readiness than one of the spindle-cell type.

(5) *The Manner in which they are held together.*—So far as regards the sarcomata at least, the more loosely the cells are held together the greater tendency there is for the tumour to recur.

(6) *Absence of any Tendency to Complete their Developmental Intention.*—Of all signs of malignancy this, in the case of the sarcomata, is perhaps the most unequivocal. The cells do not complete the connective tissue they were destined to generate. Instead of their energy being occupied in the metabolism necessary to secrete the matrix peculiar to each, it is wholly expended in causing the cell to reproduce itself.

(7) *Tendency of the Cells to Spread into Neighbouring Interfibrillar Spaces.*—In examining a tumour, the tissues round about it should be carefully investigated with a view to noticing whether its cells incline to pierce into them in long rows. If so, such a tumour is dangerous and should be excised with a wide margin. A single cell left in the surrounding parts will reproduce it. The cancer of the mamma shows more tendency to penetrate the surrounding stroma of the gland than perhaps any other tumour. It is also one of the most malignant of tumours.

Age at which they Occur.—It is said that sarcomata are the heritage of youth, cancers of old age, and perhaps this is true. It must not, however, be supposed that the former are unknown in old people. Some of the most typical sarcomata the author has met with have been taken from persons over sixty years of age.

Absence of Fat Tissue.—As a rule, adipose tissue rapidly disappears from the centre of sarcomata; their cells evidently grow from it. Masses of adipose tissue, on the other hand, are frequently seen in a cancerous tumour, because the cells proper of the tumour are epithelial, and merely pierce into the spaces between the fibres without actually springing from the fibres themselves.

General Methods of Preparation.—The majority of the sarcomata should be hardened in spirit (Hardening Solution "A." Section 36). The myxomatous sarcomata are better hardened in "C." Stain with hæmatoxylene, hæmatoxylene followed by eosin, or with picro-carmine. Mount in Farrants' solution.

The Round-Cell Sarcomata.

275. In the old nomenclature of tumours these were known as *encephaloid or medullary cancers.* The cells within them are sometimes small, at other times large.

The small round cell sarcoma is found most commonly as a growth of the subcutaneous areolar tissue, attached to bone, or springing from the neuroglia of the brain or spinal cord. It is lobulated on the surface, and somewhat flattened behind, where it presses upon neighbouring parts. In consistence it may be so soft as to resemble brain tissue; at other times it is tougher, but it is the softest of all the sarcomata. When cut into, the exposed surface appears

smooth and homogeneous, unless where some of the implicated tissues intervene. It has a pink or yellowish-pink colour, and may reach several pounds in weight.

FIG. 116.—SMALL-ROUND-CELL SARCOMA CELLS (×450 DIAMS.)

(*a*) Ordinary small round cells of the tumour; (*b*) larger polynucleated cells (Hæmatoxylene).

Like all the connective tissue tumours, it has a sharp border, and can be cleanly dissected out. A primary cancerous tumour can never be isolated in this way. There is the greatest difficulty in determining where the sound tissue ends and the cancer begins.

Its cells, as a rule, are about the size of a blood leucocyte, but some are larger—from twice to three times as large. Each of the small cells has a single large nucleus, so large

FIG. 117.—SMALL-ROUND SARCOMA CELLS INFILTRATING MUSCULAR FIBRE AT SOME DISTANCE FROM A TUMOUR OF THE TONGUE (×450 DIAMS. Hæmatoxylene.)

that it appears often to constitute the entire cell. This is never the case, however, as a delicate protoplasmic margin can always be dis-

tinguished, with careful focussing, around it. The larger cells usually have two or four nuclei, and if proper methods of examination be adopted, an intra-nuclear plexus may sometimes be detected.

The nucleus stains deeply and readily with nuclear staining reagents, such as hæmatoxylene or carmine—a character which is inherent in the cells of all actively-growing tumours.

The intercellular substance is of a granular and albuminous nature. It serves to cement the cells only loosely together, and hence the tumour is usually very soft. Where, however, the tumour is young, muscular fibres or white fibrous tissue may be mixed up with it. Blood-vessels are abundant; and being so badly supported by the soft friable tumour substance, are constantly liable to rupture. Blood extravasations are consequently often met with in these tumours.

FIG. 118.—LARGE-ROUND-CELL SARCOMA, VAGINAL WALL (×350 DIAMS.)
(*a*) Cells of the tumour; (*b*) capillary blood-vessel (Hæmatoxylene).

The degenerations to which they are liable are chiefly the *fatty* and *myxomatous*.

Preparation.—As for sarcomata generally.

276. **The large round-cell sarcoma** is much less common than the small; the cells are four or five times larger; and the nuclei are well defined, large, and multiple. The protoplasm is also very granular and cloudy. No special situations can be assigned in which they are more frequent than in others.

Preparation.—As in foregoing.

THE SPINDLE-CELL SARCOMATA.

277. *Syn.* Fibro-plastic tumour (Lebert); fasciculated sarcoma (Cornil and Ranvier); recurrent fibroid (Paget).

These are perhaps the commonest of this group of tumours, and are found more in dense fibrous textures, such as the derma, periosteum, tendons, and sheaths of muscles, than the round-cell types.

They are composed of masses of spindle-shaped cells, among which may be distinguished the following three varieties:—

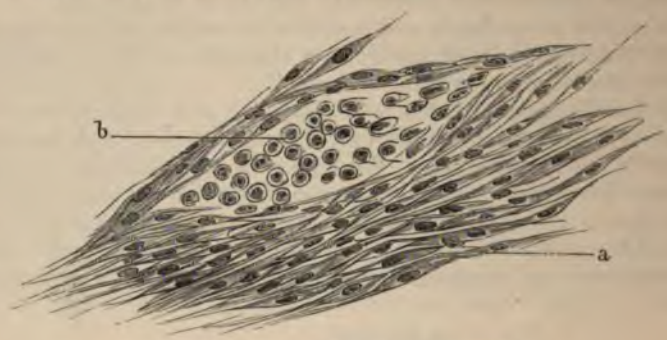

FIG. 119.—SMALL-SPINDLE-CELL SARCOMA (×300 DIAMS.)
(*a*) The spindles exposed entire; (*b*) the same cut across (Hæmatoxylene)

(1) **The Small Spindle-Cell Sarcoma.**—This is more common than the other two. Like all the spindle-cell sarcomata, it is some-

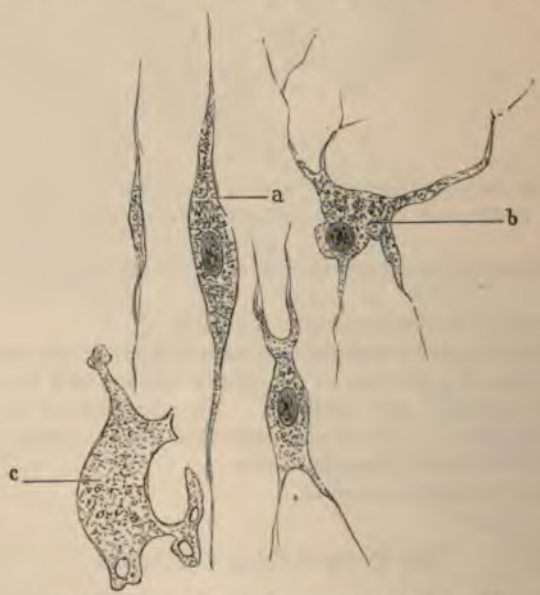

FIG. 120.—LARGE-SPINDLE-CELL SARCOMA (×400 DIAMS.)
(*a*) Ordinary spindle; (*b*) branched flat cell; (*c*) flat endothelium-like cell (Hæmatoxylene).

what tougher than the round-cell variety, but has the same sharply-circumscribed border. The cells taper towards their ends, and are

furnished with an *oval-shaped* nucleus which stains readily. The spindles interlace in bundles at somewhat obtuse angles, and these bundles are sometimes cut across in making a section. When so, the divided cells look like, and are frequently mistaken for, small round cells, especially if the section happen to pass through the middle of a bundle so as to include the nucleus. A true spindle-cell sarcoma contains very few, if any, round cells.

(2) **The Large Spindle-Cell Sarcoma.**—This differs from the former mainly in the size of its cells, which are three or four times bulkier. The nucleus, as in the foregoing, is also oval in shape. Flat, branched cells are occasionally associated with the spindles.

(3) **The Oat-seed-like spindle-cell Sarcoma.**—This is made up of very small obtusely-pointed spindles, loosely held together, and hence is a softer tumour than the two preceding.

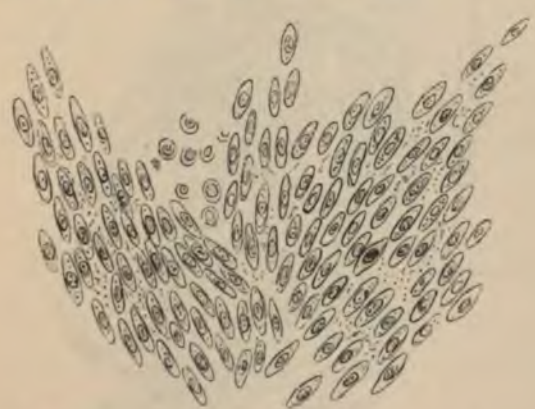

FIG. 121.—OAT-SEED-LIKE SPINDLE-CELL SARCOMA (×300 DIAMS.)

Malignancy.—This is chiefly local, although multiple spindle-cell tumours are sometimes met with widely spread throughout the various organs and tissues.

Reproduction of the Spindles.—Do the cells of these tumours pass first through a round-cell stage, or is the one spindle generated directly from the other? The fact that the tumour is usually, when a pure sarcoma, simply a mass of spindles, would point to the probability of their direct origin from pre-existing spindles; and if the tumour be carefully searched, strong evidence proving the truth of this conjecture, will be found. The one spindle seems to be reproduced from another in the following way:—The nucleus of a particular cell is noticed to become enlarged and, subsequently, slightly constricted in the middle, so as to assume a dumb-bell shape. A similar depression is noticed in the body of the cell. The nucleus completely divides into two, while the indentation in the body of the cell becomes deeper and the

junction between the two halves more attenuated and drawn out. Each nucleus retreats into a half of the cell, and the separation between the two parts of the body shortly becomes completed, two new spindles thus resulting.

Preparation.—Harden in "A"; stain in hæmatoxylene and subsequently in eosin; mount in Farrants'.

THE GIANT-CELL SARCOMATA.—*Syn.* Myeloid Sarcomata (Paget).

278. These are generally, though not always, found growing primarily from bone or periosteum. The jaws and the femur are

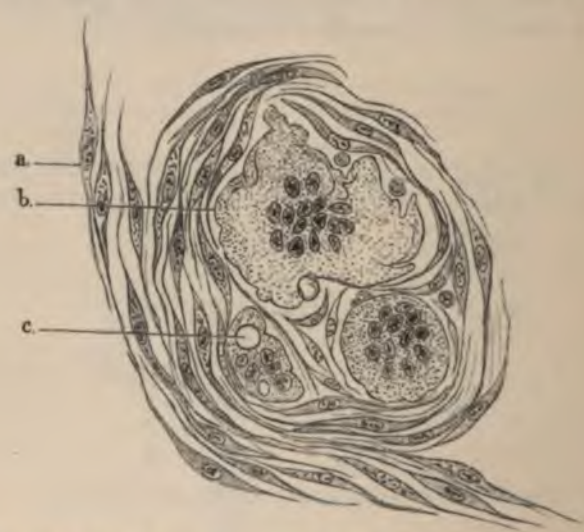

FIG. 122.—GIANT-CELL SARCOMA (MALIGNANT EPULIS) FROM LOWER JAW (×400 DIAMS.)

(*a*) Spindle-cell basis round the giant cells; (*b*) giant-cell containing many nuclei; (*c*) a vacuole in a giant cell (Picro-carmine).

among the commonest bones on which they are located. That which occurs on the jaw is known as a **malignant epulis.**

They are, as a rule, soft flesh-like tumours, but in certain instances have the fibrous fasciculated appearance of a spindle-cell sarcoma. They tend to grow into the bone to which they are attached, if of periosteal origin to begin with, so that a spontaneous fracture of a long bone or of the lower jaw may thus be caused. They all possess the property of forming abortive small pieces of bone within their substance, a gritty sensation being thus often experienced in cutting through them. It occasionally happens that they are encased in a thin shell of such newly-formed bone. Extensive hæmorrhages commonly take place into

them, and their vessels may become distended or angeiomatous. The name **fungus hæmatodes** was formerly given to the tumour when in this state.

The special feature of the tumour is the occurrence within it of the large polynucleated masses of protoplasm designated **giant-cells** or **myelo-plaxes** (Robin). Although the name myeloid is usually applied to such tumours, yet certain authors have taken exception to it on account of the cells not being exactly like those of fœtal marrow, and have restricted the application of the term to a tumour resembling that which has been described as the large round-cell sarcoma (Sect.

FIG. 123.—GIANT CELLS FORMING BONE, FROM A MALIGNANT EPULIS (×300 DIAMS.)

(*a*) The bone matrix, with granular calcic deposit; (*b*) small giant cell; (*c*) the same after dividing and when about to become converted into a bone corpuscle; (*d*) some of the surrounding spindle-cell tissue (Picro-carmine).

276). There cannot, however, be any misconception of the term *giant-cell sarcoma.*

The tumour is seldom, if ever, entirely composed of giant cells. It will usually be found that the giant cells are embedded in a matrix of spindles, and it comes to be a question whether the tumour is to be ranked as a spindle-cell sarcoma with giant cells added to it, from the fact of its having grown in connection with a bone, or as a distinct variety of sarcoma. In many cases, such as in the malignant epulis, the tumour seems to be simply a spindle-cell sarcoma invading bone, destroying it, and liberating the bone corpuscles which then develop into giant cells.

The giant cells are large, rounded, flask or irregularly shaped masses of protoplasm measuring from 50 to 120μ or more in diameter. They usually contain from twenty to thirty small oval-shaped nuclei, either clustered in a mass at the centre of the cell or arranged in a crescent at one end. They sometimes throw out lobes or branching processes, but these are not so common as in the giant cells found in tubercle. The spindle-cell tissue forms alveolar cavities in which the giant cells are contained.

Origin of the Giant Cells.—They are probably derived from two sources—the cells of the deep layer of periosteum and the bone corpuscles. The matrix of the bone becomes absorbed by the invasion of the spindle-cell tumour; the bone corpuscles are liberated and enlarge into the giant cells. These still retain the power of reproducing bone, and under certain circumstances this power is reasserted—hence the small pieces of abortive bone found scattered throughout the tumour. When the giant cell loses its sarcomatous characters and begins to revert to its natural function of forming bone, it divides into a number of smaller masses or osteoblasts. These then usually arrange themselves round a blood-vessel of the tumour and commence to throw out a calcified matrix just as in natural ossification. Ossification of the tumour, however, is never complete, and the bone seldom has the laminated character which it possesses normally.

Malignancy.—Like that of the spindle-cell sarcomata, its malignancy is chiefly local, although secondary bone-forming tumours may occur in the lung.

Preparation.—As for sarcomata generally.

Meaning of certain Terms applied to Tumours Growing from Bone.

279. It may be as well to define these explicitly, as some amount of confusion exists regarding their exact significance.

(1) **Osteo-sarcoma and Sarcoma of Bone.**—Virchow, in his work on tumours, was inclined to make a distinction between these two terms. Looked at in the light of our modern knowledge of the origin and nature of tumours, any distinction of this kind seems to be artificial and unnecessary. The two terms are literally synonymous.

(2) **Ossifying sarcoma** is a term applied to a tumour which has the power of forming pieces of bone-tissue throughout its substance whether it be connected with a bone or not. Although most of these primarily arise from bone or periosteum, yet the secondary tumours may be situated in the lung or other soft part and still retain their bone-forming propensities.

(3) **Osteoid Sarcoma.**—This is a term the author cannot understand. The terms "osteo-sarcoma" (round, spindle, giant-celled, etc.) and "ossifying sarcoma" are quite sufficiently comprehensive to include

all the sarcomatous conditions of bone. A tumour which has become converted into a tissue such as bone or cartilage is no longer a sarcoma, and ought to have a separate designation.

(4) **Osteoma, Ossifying Chondroma, and Osteo-chondroma.**—These terms are sufficiently explicit and hardly require any explanation. The *osteoma* is a mass of newly and completely formed bone. An *ossifying-chondroma* is a cartilaginous tumour with a tendency to ossify, and an *osteo-chondroma* is a cartilaginous tumour growing from a bone.

(5) **Osteo-cancer.**—Secondary cancers of bone are occasionally seen. A primary cancer of bone is a tumour unknown, and it is

FIG. 124.—MYXOMATOUS CAVITY IN THE CENTRE OF A SARCOMATOUS TUMOUR (×40 DIAMS.)

(*a*) Substance of the tumour as yet unaffected with the degeneration; (*b*) the clear myxomatous part; (*c*) a vein; and (*d*) an artery in the midst of the mucoid (Carmine).

difficult to see how such a tumour could ever arise unless from some epithelial remnant left attached to a bone during early intra-uterine existence.

SPECIAL FORMS OF SARCOMA AND SARCOMA-LIKE TUMOURS.

MYXOMATOUS SARCOMA.

280. The mucous or myxomatous degeneration is common in sarcomata, especially in such as arise from subcutaneous areolar tissue. The tumour sometimes goes by the name of a **myxoma.** It is markedly lobulated, and when cut into, a quantity of clear, ropy, mucous liquid

exudes from it. The whole mass has a trembling jelly-like consistence, and when the cut surface is examined, parts of the tumour are seen to be more gelatinous than others. There are frequently angular spaces contained in it filled with the mucous fluid. The mucin contained in the fluid is thrown down in a stringy precipitate on the addition of acetic acid.

Microscopically the tumour is most commonly a round-cell sarcoma. The myxomatous degeneration runs along the course of the blood-vessels, and the angular spaces above referred to generally contain one or more small arteries in their midst. It specially affects the intercellular substance of the tumour, any fibrous tissue which may be left

FIG. 125.—PORTION OF THE EDGE OF THE MYXOMATOUS SPACE SHOWN IN FIG. 124 (×450 DIAMS.)
(a) The edge of the tumour; (b) the branching cells lying in the clear mucoid (Carmine).

in it, and the areolar coats of arteries. These dissolve into, or at least become replaced by, the clear jelly-like substance, so that the cells of the tumour are left dissected out. The latter then begin to emit processes whereby a network of branching cells in time results with the transparent basis substance between them.

Preparation.—Harden in "C"; stain in hæmatoxylene; mount in Farrants'.

MELANOTIC SARCOMA.

281. The melanotic degeneration is also common, especially in such sarcomata as arise from surfaces naturally containing pigment, as the choroid, the skin, etc. The cells are usually of the round type, although pigmented spindle-cell sarcomata are also met with. The melanine is brown in colour when examined with transmitted light, and assumes

the form of granules. These are deposited in the protoplasm of the cell, primarily round the nucleus, and, subsequently, within it. The whole cell, in course of time, becomes filled with pigment. When the cells are young and actively dividing they have large nuclei, and are almost, if not entirely, free from pigment. It is only apparently when resting that melanine is deposited. These tumours are exceedingly

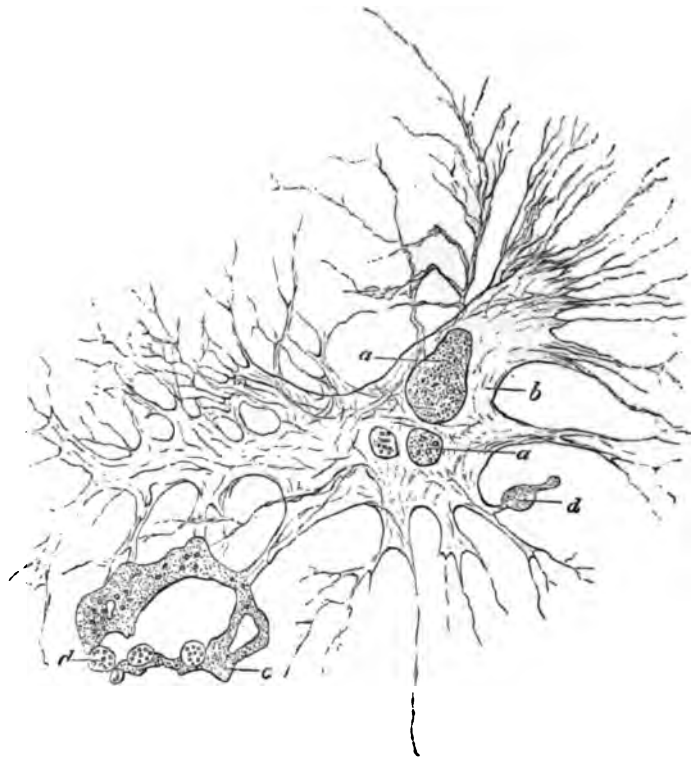

FIG. 126.—GIANT BRANCHED CELL FROM A MYXOMATOUS PAROTID SARCOMA (×450 DIAMS.) (Picro-carmine).

malignant. The primary tumour is perhaps commonest in the eyeball, the secondary tumours in the liver, lung, and skin.

Preparation.—Harden in "A"; stain in carmine somewhat faintly; mount in Farrants; or clarify and mount in dammar.

ALVEOLAR SARCOMA.

282. This is a tumour described by Billroth (No. 33) as a special variety. It consists of a delicate mesh-work of fibrous tissue, in each alveolus of which is contained a single large round connective tissue cell with one or more nuclei. Sometimes there may be two, three, or more

such cells in a single mesh. The cells are so large that in some examples of the tumour, especially those growing from bone, they look

FIG. 127.—MELANOTIC SARCOMA FROM EYEBALL (×450 DIAMS.)
(a) Cell almost completely pigmented; (b) a young dividing unpigmented cell; (c) pigmented spindles (Carmine).

like small giant cells (*sic*). Many of these so-called alveolar sarcomata seem to be simply young sarcomata in which the original stroma of the part from which the tumour has arisen has not as yet disappeared,

FIG. 128.—ALVEOLAR SARCOMA FROM SKIN OF THE BACK (×350 DIAMS.)
(a) Large sarcoma cells lying in the alveolar mesh-work; (b) a small blood-vessel (Picro-carmine).

and whose meshes are distended by the rapidly enlarging connective tissue corpuscles. An alveolar appearance may thus be readily produced.

It is said to be the nearest approach to a cancer found in any of the connective tissue tumours, but may be readily distinguished from a true epithelioma by the following characteristics:—

(1) The cells are of the connective tissue class, and are not derived from an epithelial surface.

(2) They are frequently still attached to the walls of the alveolus. The epithelial cells of a cancer never are.

(3) The meshes usually contain not more than one to four cells. In a cancer the cells contained in the meshes of the tumour are always multiple.

Preparation.—As for sarcomata generally.

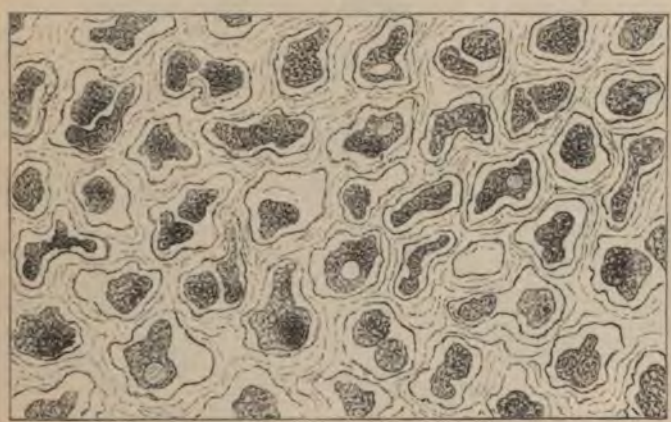

FIG. 129.—YOUNG SARCOMA GROWING FROM THE DENSE FASCIAE OF THE FRONT OF THE LEG (×350 DIAMS.)

The cells of the connecive tissue have formed an alveolar structure by enlarging and pushing the neighbouring fibrous tissues aside (Picro-carmine).

GLIOMA OR NEURO-GLIOMA—*Virchow* (γλία, *glue*).

283. These are usually small round-cell sarcomata derived from the connective tissue of the brain, spinal cord, or retina. They sometimes have a well-defined border, at other times it is almost impossible to say where the tumour supervenes upon the nerve tissue.

In certain cases they are composed of the most beautiful branching, spider, or Deiters' cells, the network produced by their interlacing processes forming an exquisite microscopic object. In chronic epilepsy, and in various other diseases of the central nervous system, hard, almost cartilage-like masses are found in the brain, either in the cortex or in the medulla oblongata. They are usually made up of a branching feltwork of these spider cells. They are liable to become fatty, calcareous, or myxomatous.

Preparation.—Harden in "C," followed by "A"; stain first by the

copper-hæmatoxylene method (Sect. 43), subsequently with carmine, clarify and mount in balsam dissolved in xylol; or stain in carmine, and half clarify in oil of cloves, mount in dammar.

FIG. 130.—GLIOMATOUS TUMOUR OF THE BRAIN FROM A BOY (×350 DIAMS.)
(a) Blood-vessel; (b) spider cell with double nucleus; (c) small round cell (Picro-carmine).

ANGEIO-SARCOMA (*ἀγγεῖον, a vessel*).

284. The term angeio-sarcoma is applied to a sarcoma in which the blood-vessels undergo more or less varicose dilatation. Extravasations

of blood take place into the substance of the tumour, and from this cause, as well as from the sudden distension of the vessels which may ensue, the tumour seems to grow with extraordinary rapidity. Lying among the extravasated blood are frequently many of the cells of the tumour.

Preparation.—As for sarcomata generally.

FIG. 131.—ANGEIO-SARCOMA OF UPPER JAW (×450 DIAMS.)

(*a*) Giant cell; (*b*) section of a varicose and distended vessel; (*c*) small-round cells of the tumour (Carmine).

CYLINDROMA.

285. The cylindroma was formerly supposed to be a cancer—that is to say, an epithelial tumour. The general opinion now, is that it is of mesoblastic origin. There is little doubt, however, that the many tumours described as *cylindromata* by various authors have differed in their structure and mode of origin. Malassez (No. 4, January, February, and March 1883),[1] in an exhaustive treatise on the subject, limits the term to a tumour of truly epitheliomatous nature with myxomatous degeneration of the stroma. Its general characters, as observed with the naked eye, are those simply of a somewhat soft sarcoma.

Microscopically, according to Billroth, it is composed of plexiform cylinders, knobs, and spheres of round cells. These push surrounding tissues aside, and as they increase in bulk, vessels are projected into them. The tumour thus comes to be composed of a number of branch-

[1] Consult for synopsis of literature of subject.

ing blood-vessels around which the cells of the tumour are arranged in

FIG. 132.—CYLINDROMA FROM BRAIN OF A GIRL SHOWING THE CELLS CLUSTERED ROUND A SMALL ARTERY AND ITS CAPILLARY (×450 DIAMS.—Carmine).

the above-mentioned manners. One special seat of these tumours is the orbit. They possess the malignancy of the sarcomata.

FIG. 133.—MYXOMATOUS CYLINDROMA, MALE BREAST (×350 DIAMS.)

(a) The branching cylinder-like rows of cells; (b) mucoid cavities of the tumour between the rows of cells. (Hæmatoxylene.)

There is also a tumour known as a **myxo-cylindroma** which occurs in various situations. The author has seen a typical example taken from the neighbourhood of the male breast.

To the naked eye it simply resembles an ordinary myxomatous sarcoma, but microscopically, differs from it in the disposition of the sarcoma cells. These, instead of forming an interlacing network by their processes, ramify in club-shaped masses or in branching rows and cylinders, between which is the clear mucous liquid.

Preparation.—As for sarcomata generally.

LYMPHO-SARCOMA (*Lymphadenoma*).

286. This name is given to a tumour which in its structure somewhat resembles a lymphatic gland. It usually commences in lymphatic glands, several members of a particular group being almost simultaneously affected. These enlarge and coalesce so that the original

FIG. 134.—LYMPHO-SARCOMA FROM THE SPLEEN (×450 DIAMS.)
(*a*) Reticulum of the tumour; (*b*) the small round cells contained in the meshes. (Carmine.)

outlines of the individual glands are lost. The mass may come to weigh several pounds.

The special sites in which they are found are, as primary tumours, in the glands of one of the mediastina, particularly that of the posterior, while the secondary tumours occur in such organs as the kidney, spleen, or liver. They may sometimes even be primary in these organs. When located in the anterior mediastinum, they may grow over and into the pericardium, so as to overlap the heart like a cap.

General Characters.—They have a sharp margin, and are somewhat lobulated, especially when they are young. The cut surface has a pinkish-yellow colour and a homogeneous aspect, unless where portions of the tumour have become fatty. Hæmorrhages occasionally take place into them. They tend to infiltrate parts, so that a bronchus, for instance, may become surrounded by the tumour mass, or the tumour may grow from the interior of the thorax through the intercostal spaces

outwards into the axilla. When they occur as primary tumours in the kidney, the tissue of the new growth insinuates itself between and around the uriniferous tubes, and gradually causes the absorption of these.

Microscopically they are found to be composed of a delicate fibrous reticulum, in the meshes of which lie numbers of cells like those of a small round-cell sarcoma, only not possessing, as a rule, such a prominent nucleus. The reticulum somewhat resembles that of a lymphatic gland, hence the name "lymphadenoma."

Development.—They appear to be sarcomata, with this peculiarity (according to Cornil and Ranvier), that certain of the cells have the power of reproducing fibrous tissue. This constitutes the reticulum, the meshes of which in course of time become distended with the remaining cells of the tumour. The tumour seems to hold a place intermediate between a round-cell sarcoma and a fibrous tumour.

Preparation.—Harden in "C"; cut very thin sections; stain in hæmatoxylene; brush out the stroma, and mount in Farrants'; or mount in Farrants' and squeeze down the cover glass.

287. **Hodgkin's Disease, Adenia** (Trousseau), **Lymphoma** (Ziegler).—In connection with lympho-sarcoma it may be as well to refer to this disease, which in all probability is totally different in its nature from the foregoing, but which is often confounded with it. In the year 1832 Hodgkin (No. 34, xvii.) described a peculiar disease in which the lymphatic glands throughout the body undergo universal enlargement, a condition which is accompanied by great anæmia. There is no doubt that Hodgkin included many other enlargements of glands, such as the strumous, in the same category; but there is nevertheless a distinct disease in which a peculiar and universal enlargement of the glands takes place, which is unconnected with the strumous diathesis, and which is not an effect of local causes of irritation. It is this which is understood at the present day as Hodgkin's Disease.

The enlargement of the glands is uniform and universal, and they have a pinkish gray colour when incised. Long strings of them may be seen running along the course of the aorta, or in the neck, groins, and axillæ; and in situations where lymph glands are almost imperceptible in health, they become so prominent as to be distinctly felt through the skin.

The enlargement seems to be due to an excess of what looks like the normal reticulum of the gland, with an increased number of lymph corpuscles lying in the meshes. The glands do not tend to coalesce as in true lympho-sarcoma, and, altogether, the affection looks more like a lymph-adenitis due to some wide-spread cause, than a disease of a truly sarcomatous nature.

Lipomatous Sarcoma.

288. It has been said, in the general description of the characters of the sarcomata, that if they arise from a part containing adipose

tissue, the latter tends to disappear wherever the tumour grows. The fat cells are evidently converted into those of the sarcomatous growth, and in doing so, lose their fat-forming properties.

FIG. 135.—CELLS FROM A LIPOMATOUS SARCOMA (×450 DIAMS.—Carmine and Perosmic Acid.)

It occasionally happens, however, that the fat-forming tendencies of the cells of the tumour reassert themselves, so that their protoplasm becomes loaded with oil globules. The condition is not a fatty degeneration, but an infiltration like that of a fatty liver. The name "lipomatous sarcoma" is given to such a growth.

In outward appearance it presents no feature different from that of a round-cell sarcoma, but when examined microscopically, the infiltration of the cells of the tumour with oil becomes apparent. It is almost always situated in the subcutaneous areolar tissue.

Preparation.—Harden in "A"; stain in perosmic acid, followed by picro lithium-carmine; mount in Farrants'.

PSAMMOMA (ψάμμος, *sand*).

289. This should not be placed among the sarcomata, as undoubtedly it does not belong to them. For want of a better means of classifying

FIG. 136.—PSAMMOMA FROM CHOROID PLEXUS (×300 DIAMS.)
(*A*) Branching vessels with the cell-nest-like bodies upon them; (*B*) cell nests calcified. (Picro-Carmine.)

it the author has included it among the sarcoma-like tumours. It is a tumour of varying size found growing from the choroid plexus, the ventricles of the brain, the arachnoid, and dura or pia mater, whose special characteristic is that it contains sand-like concretions.

The tumour is made up of a series of endothelium-like cell nests arranged round blood-vessels, which in course of time become infiltrated with calcareous salts. It is called an "angeio-lithic sarcoma" by Cornil and Ranvier on account of its connection with the blood-vessels.

Preparation.—As for sarcomata generally.

Degenerations of the Sarcomata.

290. (1) **Fatty.**—They are all liable to this, as may be easily understood from the large bulk of tissue which has to be nourished—often by a comparatively scanty supply of blood.

(2) **Calcareous.**—This sometimes follows upon the fatty.

(3) **Ulcerative.**—When the tumour comes to the surface, the skin is apt to give way, and the tumour begins to ulcerate and granulate. Large fungating masses are thus constituted, as the vessels, so soon as they are liberated from the pressure exerted upon them by the skin, swell out into granulation loops.

(4) **Fibrous.**—This can hardly be called a degeneration, and it is to be regretted that it does not occur oftener than it does. Were the tumour converted into an inert mass of fibrous tissue, little further trouble would be experienced from it. It is not known as yet what prevents this taking place.

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CHAPTER XXV

THE NEW FORMATIONS AND TUMOURS—(*Continued*)

MESOBLASTIC TUMOURS—GROUP II

THE SIMPLE HISTIOID NEOPLASMATA

291. THESE all originate, like the sarcomata, from a derivative of the mesoblast. They differ from the sarcomata in so far as they are constituted of fully developed connective tissue, such as fibrous tissue, bone, cartilage, etc.; and also in the fact that, generally speaking, they are non-malignant.

Definition.—*A class of tumours springing from a mesoblastic derivative, and consisting of tissues resembling the fully formed simple tissues of the body.*

FIBROUS TUMOUR (*Fibroma*).

292. **Definition.**—*A tumour composed of white fibrous tissue.*

So far as is known, yellow elastic tissue never forms a neoplasm, nor does it appear to be reproduced in the majority of pathological new growths such as cicatrices, or the new tissue of cirrhotic organs. Elastic fibres may be dragged into a cicatrix, but do not seem to arise in it *de novo*.

Sites.—It can be said that these, like the sarcomata, may grow wherever fibrous tissue exists. The commonest sites, however, are in tough, dense, fibrous tissues, such as the derma of the skin, sheaths of tendons, fasciæ, mucous membranes, etc.

Description.—They have a sharp border, and can be dissected out of the part in which they are located. They are hard, dense, and leather-like as a rule, but when they grow from a mucous membrane, they frequently become œdematous, which gives them a soft velvety consistence. On section, the exposed surface shows a number of fibrous bands interlacing in all directions without any definite arrangement. They have a gray or pinkish colour, and, in growing, push neighbouring parts aside, so that the latter come to form a spurious capsule for the growth.

Microscopically, they are made up of wavy bundles of white

fibrous tissue interlacing in all directions, and specially surrounding blood-vessels. On each bundle lies an oval or fusiform connective tissue nucleus, as on any other fibrous tissue. The younger or growing parts of the tumour usually show a vast number of young connective-tissue cells of round or oval shape. When such is the case, the tumour is sometimes called "fibro-cellular;" the cells representing the young material from which the fibres are secreted. They all tend to form fibrous tissue, and hence are not sarcomatous.

Malignancy.—As a rule, fibrous tumours, especially if they have reached maturity, are benign growths. It must be remembered, how-

FIG. 137.—FIBROUS TUMOUR FROM THE ANTRUM OF HIGHMORE (×450 DIAMS.)
(a) Fusiform nucleus; (b) younger nucleus of an oval shape; (c) isolated fibroblast (Hæmatoxylene).

ever, that when young they are very closely related to the sarcomata, and will certainly recur if only partially excised.

Degenerations.—These are chiefly the myxomatous, angeiomatous, and œdematous. In the myxomatous, the fibres of the tumour become beautifully dissected out, and show a delicate wavy outline. In the angeiomatous, the blood-vessels are much dilated, and their areolar coats being connected with the rigid fibrous tissue of the tumour, it is with great difficulty that they contract when wounded; hence the hæmorrhage is sometimes excessive. Fibrous tumours which grow from mucous membranes into a cavity such as that of the nares, are always liable to become œdematous. They then constitute what are known as mucous polypi.

Preparation.—Harden in "A"; stain in logwood followed by eosin, or in perosmic acid followed by picro-carmine; mount in Farrants'.

293. **Fibrous Neuroma.**—The true neuroma is described under the "Compound Histioid Tumours." Small fibrous tumours are, however, occasionally found on the trunks of nerves and around nerve terminations in stumps. They are mere fibrous masses, sometimes encircling the bundles of nerve fibres, at other times simply lying upon them. They give rise to great pain, especially when they grow to any size in a stump.

Preparation.—Harden in "A"; stain in perosmic acid and in picro-lithium carmine; mount in Farrants' solution.

294. **Molluscum Fibrosum** (*molluscus, soft*).—This is also a fibrous growth, one peculiarity being the fineness of the fibrous tissue composing the tumour. The tumours are pendulous polypus-shaped

FIG. 138.—MYXOMATOUS FIBROUS TUMOUR OF THE DEEP FASCIA OF THE NECK (×450 DIAMS.)
Shows the wavy fibres dissected out, and each with a flat nucleated corpuscle upon it (Picro-carmine).

bodies growing from the skin, and are usually multiple. They are sometimes diffusely scattered as a skin eruption.

Preparation.—As for fibrous tumour.

THE FATTY TUMOUR (*Lipoma*, λίπος, *fat*).

295. **Definition.**—*A localised hypertrophy of fat tissue.*

Sites.—They are most common in the subcutaneous fat tissue, especially on parts which are pressed upon, such as the buttocks or shoulders. They are rarer in internal parts, but are sometimes found in localities such as the peritoneum, pleura, and heart. They also sometimes grow from synovial membranes in the form of bunches of villus-like processes which project into the joint. The tumour in this case actually arises from the synovial fringes of the subepithelial fibrous tissue. The so-called *lipoma of the nose*, a large pendulous mass, is in reality a fibrous growth—a localised elephantiasis.

Description.—They consist of lobulated masses of fat tissue with a sharp border, and are to a certain extent encapsuled within the surrounding parts. They can frequently be dragged out entire from the capsule in which they lie. When examined microscopically, the fibrous tissue within them is usually more abundant than in adipose tissue, but otherwise they present no marked divergence from the structure of ordinary fat.

Malignancy.—As a rule they are quite benign, but cases have been recorded (Spence) in which they have assumed a malignant character probably from becoming sarcomatous.

Preparation.—Harden in "A"; stain lightly in perosmic acid, followed by picro-carmine; mount in Farrants'. The fat may be partly dissolved out in a mixture of equal parts absolute alcohol and ether.

CARTILAGINOUS TUMOURS (*Chondromata, χόνδρος, cartilage*).

296. **Definition.**—*Masses of new tissue composed either of hyaline or white fibro-cartilage.*

The Hyaline Cartilaginous Tumour. *Sites.*—This is usually met with growing from bone, not from cartilage, and the favourite sites are prominences of bone, such as the acromion or coracoid processes, the ends of the clavicle, and the bones of the fingers and toes.

Description.—They are rounded lobulated tumours of very dense consistence which often appear to be encapsuled, from having compressed neighbouring parts. Tendons are frequently displaced in this way, and become stretched over the surface of the tumour. When cut into, they have the pearly bluish-pink aspect of fresh cartilage.

Microscopically they are seen to be composed not of a uniform dense cartilaginous mass, but of islands of cartilage surrounded by fibrous septa. The islands are usually not larger than a line to a line and a half in diameter, and are rounded in shape. The blood-vessels for the nourishment of the tumour run within the fibrous septa, but the cartilage masses themselves are devoid of vessels. The cartilage matrix is hyaline unless where it abuts upon the fibrous septa. Here it usually has a more or less fibrous character. Within the matrix are the *lacunæ* containing the cartilage cells. These are very much like the *lacunæ* found in healthy cartilage, and are either rounded or oval in shape. Numbers of concentric markings are seen in the matrix round about them, probably due to an oblique section of the laminæ of which it consists (Thin). The interior of the lacuna is lined by a membrane-like structure, and after death the cell usually shrinks so as to fill perhaps only a third or a half of the space. The cartilage cell is a little mass of protoplasm of irregular shape, not infrequently containing oil globules.

The lacunæ of the matrix are occasionally branched so as to cause the appearance of a series of stellate spaces with the cartilage cell lying

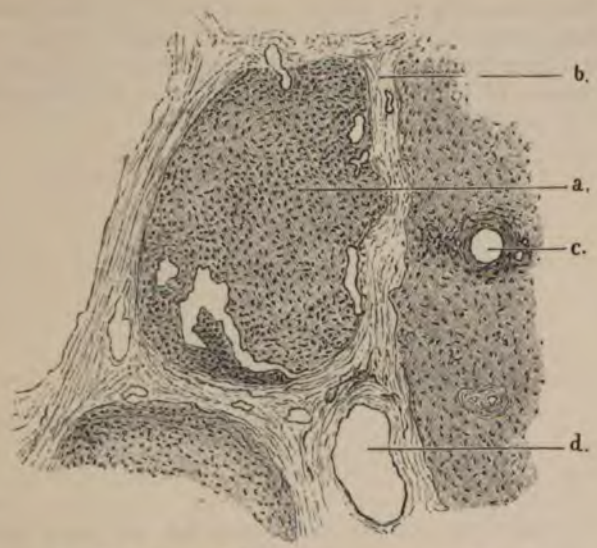


FIG. 139.—HYALINE CHONDROMA FROM SCAPULA (×50 DIAMS.)
(*a*) Island of cartilage ; (*b*) a fibrous septum ; (*c*) a small artery ; (*d*) a vein

FIG. 140.—EDGE OF HYALINE CHONDROMA ADJACENT TO A SEPTUM, SHOWING THE TRANSITION FROM FIBROUS TISSUE INTO THE HYALINE MATRIX (×400 DIAMS.)

(*a*) Connective tissue corpuscle becoming converted into a cartilage cell ; (*b*) cartilage cell ; (*c*) a group of cartilage cells in a single space (Perosmic acid).

in their centre. They have sometimes been regarded as "branched cells." They resemble the lymph spaces found in the cornea. In certain chondromata they are more abundant than in others.

Fibro-Chondromata. *Sites.*—These occur more particularly in the capsules of joints and in the ligamentous structures adjacent

FIG. 141.—SO-CALLED BRANCHED CELLS OF A CARTILAGINOUS TUMOUR OF PAROTID (×450 DIAMS.) (Picro-carmine.)

to the parotid gland. The latter is perhaps the commonest site, and the tumour as it enlarges grows into the parotid gland and becomes bound up with the gland substance. It often reaches the size of a hen's egg.

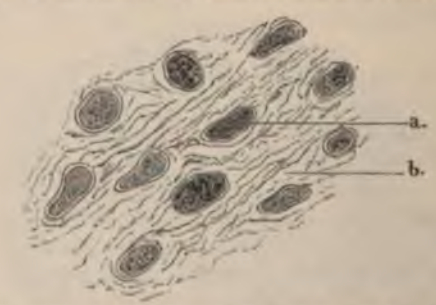


FIG. 142.—FIBRO-CHONDROMA FROM CAPSULE OF KNEE (×400 DIAMS.)
(*a*) Cartilage cells; (*b*) the matrix.

Description.—They are not so sharply circumscribed as those of the hyaline variety. They have more elasticity than fibrous tissue, are not so dense as a hyaline chondroma, and on section, the lustre is not so pearly as that of the hyaline, although it is more so than that of a fibrous tumour.

croscopically, the tumour is not subdivided into islands of cartilage like the foregoing, but is a uniform mass composed of white fibro-

cartilage. The matrix consists of white, faintly fibrous, tissue, and embedded in it are the cartilage cells. In those removed from the parotid, it may happen that pieces of hyaline cartilage are here and there to be found in the otherwise fibro-cartilaginous mass. The cells frequently contain oil globules.

Tumour composed of Embryonic Cartilage.—Young cartilaginous tumours are frequently composed of a tissue identical with the *cellular cartilage* of the embryo, and, when in this condition, closely resemble sarcomata in their microscopic features. It will generally be found, however, that the true nature of the tumour betrays itself, in some part, by the hyaline character of the matrix.

Malignancy of Chondromata.—As a rule, it may be said that where the tumour has become stable—that is to say, has reached a resting state—it is non-malignant. When they are young and growing, however, they may recur locally if any small portion of the tumour is left, or, it is even said, they may form secondary tumours in distant organs, such as the lung.

Degenerations.—These are chiefly (1) the myxomatous; (2) the calcareous; (3) osseous. The fibro-chondroma of the parotid is very frequently myxomatous, and shows the peculiarly characteristic gelatinous surface when cut into. The chondroma which grows from the end of the femur has a great tendency to ossify (*Ecchondrosis ossificans*—Virchow).

Preparation.—All chondromata may be hardened in "A"; stained in perosmic acid, Condy's fluid, or hæmatoxylene followed by carmine; and mounted in Farrants'.

TUMOURS OF BONE (Osteomata—*ὀστέον, a bone*).

297. **Definition.**—*A tumour-like mass of bone developed by a process of growth without the occurrence of inflammation.*

They were formerly known as *exostoses.* Virchow (No. 35) divides them into three classes:

(1) *Osteoma durum* or *eburneum.*—The ivory-like exostosis.

This is found chiefly on the vault of the skull or growing from the wall of the external auditory meatus, into the frontal sinuses, or into the brain. That on the outside of the skull is the most characteristic. It is round in shape, and about the size of a hazel nut or large pea; it is usually sessile, but pedunculated tumours of this kind are also met with. It is composed of laminæ of dense bone, beneath which a cancellous tissue like the diploë is sometimes found (Paget).

(2) *Osteoma spongiosum.*—This usually takes origin from the epiphyses of bone, more especially long bones, such as the femur, tibia, fibula, and humerus. The author has seen a case under the care of Mr. Joseph Bell, where almost every bone in the body had one or more of these outgrowths attached to it. It appears to originate in cartilage, which subsequently becomes ossified. A capsule of cartilage is usually

left outside, which goes on growing, while the interior is converted into bone. The bone presents a cancellous texture like that of an ordinary spongy bone. It is usually a rounded mass with a pedicle which binds it to the part from which it grows, but sometimes the tumours are sharply acuminated with a broad sessile attachment.

(3) *The Osteoma Myeloides* is simply a variety of the foregoing, in which the cancellous spaces become filled with marrow.

Osteomata sometimes grow from parts other than bone or cartilage, such as fasciæ and tendons. They constitute irregularly spicular masses moulded into their particular form by the interfibrous spaces into which they project. Such are the "drill" bones of the deltoid region.

Malignancy.—The osteomata, as a rule, do not tend to recur when removed.

Preparation.—Harden in "C"; decalcify; stain in picro-lithium carmine; mount in Farrants'.

Odontomata (ὀδούς, *a tooth*).

298. These are tumours composed of a tissue like tooth, and have been occasionally found growing from a tooth. They are true ivory outgrowths consisting of a mass of dentine.

Tumours of Muscle, Myomata (μῦς, *a muscle*).

299. They are chiefly composed of non-striated muscular tissue, but a rare congenital tumour also occurs in which the fibres are striated.

The Nonstriated Myoma (Leiomyoma). *Sites.*—It occurs chiefly in parts where muscular tissue is naturally present, as the uterus or gastro-intestinal canal, and sometimes in the prostate of old people.

The Uterine Leiomyomata may be either multiple or single, generally the former. They are hard, elastic, rounded, or kidney-shaped masses, and the cut surface has a fasciculated appearance, sometimes, without definite arrangement, at others, concentrically twisted so as to resemble the section of a ball of cotton. Where a bunch of them exists, some of the individual members may sometimes be enucleated from the basis in which they lie.

In relation to the uterus they occupy usually one of three situations; sometimes, they may be present in all three. (1) They may be embedded in the wall of the organ without projecting much either inwards or outwards. (2) They may grow into the uterine cavity, and when pediculated go clinically by the name of *fibrous polypi*. (3) They may grow into the abdominal cavity, carrying with them a layer of peritoneum. In the last situation the pedicle usually becomes much drawn-out and elongated, so that the tumour may lie at some distance

from the uterus in which it originated. It is sometimes shaped like an ovary, and may be mistaken under such circumstances for a tumour of that organ. Many of the myomata which are said to grow from the ovary are in reality of uterine origin.

Microscopically, they are mainly constituted of a mass of unstriated muscular tissue. The spindles of which the fibres consist are attenuated bodies, and are closely plaited together and adherent by what seems to be a little cementing material. They have an elongated rod-shaped nucleus which stains brightly with carmine and logwood. It should be noted that the spindles of this tumour are to be distinguished from those of a spindle-cell sarcoma by their delicacy, and also by the fact that the nucleus is rod-shaped, not oval. Between

FIG. 143.—MYOMA OF THE UTERUS (×350 DIAMS.)

(*a*) Bundles of unstriated muscular fibres; (*b*) hyaline matrix with branched spaces or cells; (*c*) muscular fibres cut across; (*d*) a blood-vessel (Carmine and glacial acetic acid).

the muscular fibres is an almost mucoid-looking connective tissue which serves to bind the bundles together. It possesses a clear matrix, in which are a number of branching stellate cells.

Blood-vessels are often abundant and sometimes so dilated that when the tumour is wounded it may bleed profusely. Like those in the fibrous tumour, they are intimately bound to the substance of the growth, so that unless the tumour tissue contracts, they can with difficulty close. The beneficial effects of ergotin in the treatment of hæmorrhage from these tumours is probably to be explained by its causing contraction of the muscular mass.

Degenerations.—(1) Calcareous, forming "wombstones." (2) Fatty is not uncommon in those which project into the uterine cavity. When this occurs, huge masses of the tumour may slough off and

be discharged *per vaginam*. (3) Blood-angeiomatous. (4) Lymphangeiomatous degeneration may cause the presence of numbers of cyst-like bodies throughout the substance of the tumour.

The intestinal leiomyomata are usually multiple. The whole alimentary canal may be the subject of them. They usually form almond-like swellings situated in the muscular coat, or they may project as polypi into the canal.

Preparation.—Considerable care is necessary to bring out the structure of the unstriated myoma. A young tumour should be chosen, as the nuclei are always better seen in this than in those which are older. Harden in "A"; stain the section deeply in ammoniacal solution of carmine; wash in water, or in water slightly acidulated with acetic acid, and treat the section with glacial acetic acid on the slide until it swells and becomes transparent. Remove the acetic acid round about the preparation; mount in glycerine jelly, and squeeze down the cover-glass forcibly with the handle of a needle.

The Striated Myoma (Rhabdomyoma.—Zenker).—Tumours containing striated muscular fibre have been described by Eberth (No. 13, lv. p. 518), Marchand (No. 13, lxxiii. p. 289), Cohnheim (No. 13, lxv. p. 64), and others. They usually grow in connection with the kidney, sometimes in the testis, and are always congenital. They are very much rarer than the foregoing variety.

They appear to bear out the character of myosarcomata, *i.e.* the tumour is mainly composed of spindle-cell tissue, some of the cells of which show the transverse striation of muscular fibre. They have, moreover, an oval nucleus.

Preparation.—Harden in "A," and stain in hæmatoxylene; mount in Farrants' solution.

Painful Subcutaneous Tubercle (Wood).

300. This is a little tumour found in the subcutaneous fat tissue, and its peculiar feature is that when touched, even lightly, pain of an agonising character is experienced. It is commonly located on the extremities, and occurs more frequently in females than males (23 to 5, Paget). It is seldom larger than a horse bean or pea, and is sharply circumscribed. The skin may be adherent to the surface, and when so, has a polished glossy appearance. On section the tumour is delicately fibrous, the fibres being at times concentrically arranged; and the remains of an old blood-extravasation, in the form of pigment crystals, is occasionally seen in its midst. A trunk of a cutaneous nerve may sometimes be found closely adherent to the tumour. A sweat gland is occasionally involved in it (Hoggan).

They appear to result not infrequently from injury to the part. It seems as if an effusion of blood took place as a result of the injury, which, in course of time, became encapsuled by fibrous tissue, thus constituting the tumour. There is little doubt, however, that they

may originate in several ways, the main point, and the peculiarity of the tumour, being that it forms an attachment to a cutaneous nerve.

Preparation.—Harden in "A"; stain in perosmic acid; mount in Farrants'.

Literature on Simple Histioid Tumours.—Consult literature of various organs, and :—**Falck**: Beitrag. z. Lehre u. Casuistik d. Bindegewebsgeschwülste d. Halses, 1887. **Haumann**: Ueb. Gelenklipom, etc., 1887. **Heerding**: Ueb. d. Fibrome d. Bauch decken, 1887. **Hénocque** (Chondroma): Dict. Encycl. d. Sc. méd., xxxiv. 1887, p. 401. **Howitz**: Ueb. Enchondrome, etc., 1886. **Hutchinson** (Subperitoneal Lipoma): Brit. Med. Journ., 1885, ii. p. 1065. **Mackenberg**: Ueb. intermusculäre Lipome, 1887. **Marchand** (Striated Myoma): Arch. f. path. Anat., C., 1885, p. 42. **Meerbeek**: Ueb. multiple Lipome, 1887. **Sutton** (Lipoma): Med. Chir. Trans. Lond., lxviii. 1885, p. 293. **Treves** (Congenital Chondroma of Neck): Brit. Med. Journ., 1887, ii. p. 993. **Vidal** (Myoma): Journ. Cutan. and Ven. Dis., N. Y., iii. 1885, p. 260.

CHAPTER XXVI

THE NEW FORMATIONS AND TUMOURS—(*Continued*)

MESOBLASTIC AND EPIBLASTIC TUMOURS

THE COMPOUND HISTIOID NEOPLASMATA

301. **Definition.**—*By such the author means to specialise tumours composed of or constructed upon the type of a compound tissue-element, such as a blood-vessel, a lymph-vessel, or a nerve trunk or ganglion.*

FIG. 144.—PORTION OF A NEUROMA FROM RIGHT EAR (BRUNS).

TUMOURS COMPOSED OF TRUE NERVE TISSUE (Neuromata).[1]

It was for long doubted whether there was such a thing as a tumour composed of true nerve elements. The majority of neuromata (Sect. 293) are simply fibrous tumours lying along the course of a nerve or attached to the nerve terminations in a stump. There cannot be any doubt, however, that true neuromata are sometimes, although rarely, found.[2]

Sites.—They are most common on the ears, eyelids, and side of the face, and Schmidt has recorded one growing from the intercostal nerves. They usually have a varicose or cirsoid appearance when dissected out, and can be readily felt in their ramifications under the skin. They grow in connection with the trunk of

[1] This tumour is of course, strictly speaking, of epiblastic origin.

[2] See cases recorded by Lorretz (No. 13, xlix. p. 435), Bruns (No. 13, l. p. 80), Marchand (No. 13, lxx. p. 36), Schmidt (No. 36, ii. p. 108).

some nerve, such as an intercostal branch, and are only moderately painful on pressure. They may reach the size of a hen's egg.

Structure.—There is in all of them a basis of fibrous tissue through which run bands of nerve fibres, some of them completely medullated, others only partially so. Large ganglion cells, with characteristic nucleus and nucleolus, are also sometimes found embedded in the tumour mass.

The nerve fibres are supposed to be developed by the junction of the ends of long spindles in continuous rows.

TUMOURS COMPOSED OF DILATED VESSELS (Angeiomata).

Definition.—*By an angeioma is meant a tumour composed of dilated vessels (ἀγγεῖον, a vessel). They may be derived either from blood or lymph vessels. The former are known as the blood-angeiomata, the latter as the lymph-angeiomata.*

The Blood-Angeiomata.

302. Two varieties of these tumours are met with—

(1) **Those developed from a simple varicose distension of Capillaries and Veins** (Plexiform or Telangiectatic).

They are the commoner of the two, and constitute the class of tumours known as nævi and "mothers' marks." Their favourite sites are the skin of the face and the orbit.

Characters.—They are flattened or slightly pendulous tumours having a blue, pink, or purple colour. They can sometimes be emptied of their blood, sometimes not. They essentially consist of extremely dilated and varicose blood-vessels, between which is an inconstant quantity of fibrous tissue. They are congenital, whereas, there is good reason for believing, that the cavernous angeiomata are not. The difference in colour, varying from a pink to a livid tint, depends, according to Billroth (No. 33), upon whether the affected vessels be situated superficially or deeply. If they are superficial, the tumour has a pink colour, if deep, it has more or less of a blue tint.

Depth of the Dilatation.—As a rule, the distended vessels do not penetrate beyond the subcutaneous cellular tissue, but they may extend into the underlying muscles. When the tumour is emptied of blood it is colourless. The vessels are arranged in small lobules from the size of a hemp seed to that of a pea, consisting of dilated capillaries arranged round sweat ducts, sebaceous glands, or hair follicles (Billroth).

Preparation.—Harden in "A;" stain in hæmatoxylene and eosin spirit; clarify, and mount in solution of gum dammar.

(2) **The Cavernous Angeiomata.**—They are mainly tumours of the liver, but similar new formations are occasionally met with in the spleen and kidney.

Those in the liver are frequently multiple, and may be so numerous

that the whole liver substance is beset with them. They have a livid colour when seen projecting on the surface, with a sulcus or depression at the margin. In size they vary from a pea to a filbert, and are more numerous superficially than in deeper parts.

When cut into, they very much resemble a blood-clot, but a stream of water allowed to fall upon the surface does not entirely remove the tumour. It washes out the blood, but leaves the trabecular network in the form of a fibrous-looking residuum.

FIG. 145.—CAVERNOUS ANGEIOMA, LIVER (×350 DIAMS.)
(a) Liver cells at margin of the tumour; (b) blood contained in the cavernous spaces; (c) walls of the cavernous spaces (Carmine).

Microscopically they are found to be composed of a tissue almost identical with that of the corpus cavernosum penis, *i.e.* of a trabecular network of fibrous tissue, enclosing cavernous spaces whose walls are lined by endothelium. Through these spaces the blood circulates as in the corpus cavernosum. There is often a little spindle-cell tissue in the walls, evidently unstriated muscular fibre. Towards the centre of the tumour, a dense mass of cicatricial tissue is not unfrequently to be found, sometimes with a little concretion in it. According to Virchow and Maier, they can be injected from all three vessels of the liver.

Preparation.—As in the telangiectatic.

The Lymphangeiomata.

303. These are generally found in the subcutaneous or submucous tissues. The lymph scrotum which accompanies filarious disease of

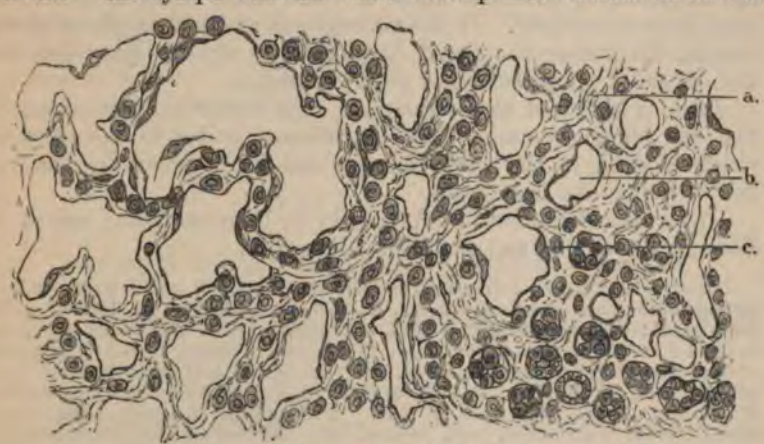


FIG. 146.—LYMPHANGEIOMA OF ORBIT (×350 DIAMS.)
(*a*) Stroma of the walls of the cavernous spaces; (*b*) a cavernous lymphatic space; (*c*) endothelium lining the space (Hæmatoxylene).

FIG. 147.—LYMPHANGEIOMA OF TONGUE (×50 DIAMS.)
(*a*) Lymphadenoid deposits; (*b*) a cavernous lymphatic space; (*c*) muscular fibres of tongue; (*d*) a small artery (Picro-carmine).

the blood; the peculiar swellings which are found in the tongue in *macroglossia* or in the lip in *macrocheilia*, are also of this nature; while elephantiasis Arabum seems in many cases to have a similar structure.

Structure.—They consist of a series of branching, varicose, and dilated lymph-vessels lined by endothelium, which, in a section, are usually empty, but during life are distended with lymph. These push the neighbouring muscular fibres or other tissue elements aside, and cause them to atrophy. In the macroglossia or lymphangeioma of the tongue, the author has found *lymph-adenoid deposits* lying between the distended lymph-vessels in great abundance.

Little is known of their causation. The theory has been advanced that the lymph scrotum of filarious disease is due to the parasitic worms blocking up the lymph-channels and hence preventing the free flow of lymph (see Sect. 245).

Preparation.—Harden in "A"; stain in hæmatoxylene; mount in Farrants', or clarify, and mount in dammar lac.

Literature on Compound Histioid Tumours.—Consult lit. of various organs, and :—**Arnozan** (Plexiform Neuroma): Journ. de Méd. de Bordeaux, xv. 1885-6, p. 72. **Ben-Israel:** Ueb. Lymphangiome, 1885. **Chevinsky** (Case of Multiple Angiomata in Child 6 mos. old): Arch. de Physiol., vi. 1885, p. 553. **Fleming** (Extensive Angeioma of Upp. Extremity): Glasg. Med. Journ., xxiv. 1885, p. 51. **Lahmann** (Multiple Neuromata): Arch. f. path. Anat., ci. 1885, p. 263. **M'Burney** (Congenital Angeiomata): N. Y. Med. Journ., xliii. 1885, p. 555. **Middeldorpf** (Lymphangeioma Cavernosum): Arch. f. klin. Chir., xxxi. 1884, p. 590. **Nauwerck** (Capillary Angeioma): Arch. f. path. Anat., cxi. 1888, p. 211. **Pieper:** Ueb. Lymphangiectasia colli congenita, 1887. **De Schweinitz** (*nævus pigmentosus*): Phila. Med. Times, xv. 1884, p. 441. **Sims** (Neuromata of Abd. Walls): N. Y. Med. Journ., xliii. 1886, p. 329. **Westphalen** (Multiple Fibrous Neuromata): Arch. f. path. Anat., cx. 1887, p. 29. **Yersin** (Angeiomata of Base of Tongue): Arch. d. Physiol. norm. et path., vii. 1886, p. 428.

CHAPTER XXVII

THE NEW FORMATIONS AND TUMOURS—(*Continued*)

TUMOURS OF EPI- AND HYPOBLASTIC ORIGIN

WARTS, HORNS, ADENOMAS, CANCERS, ETC.

304. THE whole of the true epithelia, with, perhaps, the exception of that of the kidney, are derivatives either of the epi- or hypoblast. That of the epidermis, the central neural canal, and the mouth are epiblastic, while the hypoblast forms that of the gastro-intestinal tract, bronchi, bile and pancreatic ducts.

The cancers all arise from epithelial surfaces, and, hence, if a part does not contain epithelium, it may practically be concluded that a *primary* cancerous tumour will not be found growing from it. A secondary cancerous tumour may of course form in almost any tissue.

305. **Epithelium and Endothelium.**—It will be well to settle what these two terms mean before proceeding further. A distinction between the two, founded upon their histological features, has been sometimes attempted. The endothelia are said to be flat delicate cells lining cavities, while the epithelia are usually coarser, and cover exposed surfaces. This definition will not hold good for certain epithelia, such as that covering the lung, which are as delicate as an endothelium, and closely resemble it in other structural characters. The only distinction that can be made, seems to be based upon their origin. All the epithelia, with the single exception already referred to, are of epi- or *hypoblastic* origin, while all the endothelia are of *mesoblastic* origin. This is the essential difference between them, and it matters not what morphological characters they present. Both cover free surfaces, the chief of those covered by endothelium being the pleura, peritoneum, and the interior of blood-vessels and lymphatics, while those covered by epithelium are the skin and mucous membranes, ducts and acini of glands, etc. The endothelia, therefore, are of the connective tissue class of cells, and the neoplasmata that arise from them also preserve this type.

WARTS (Verrucæ, Papillomata).

306. Several varieties are met with—

(1) *V. vulgaris* (Neumann). Small, hard, crescentic or conical excrescences, arranged in groups, or isolated, and occurring chiefly upon the hands, feet, face, and ears.

(2) *V. filiformis.* An almost thread-like excrescence usually found upon the eyelids.

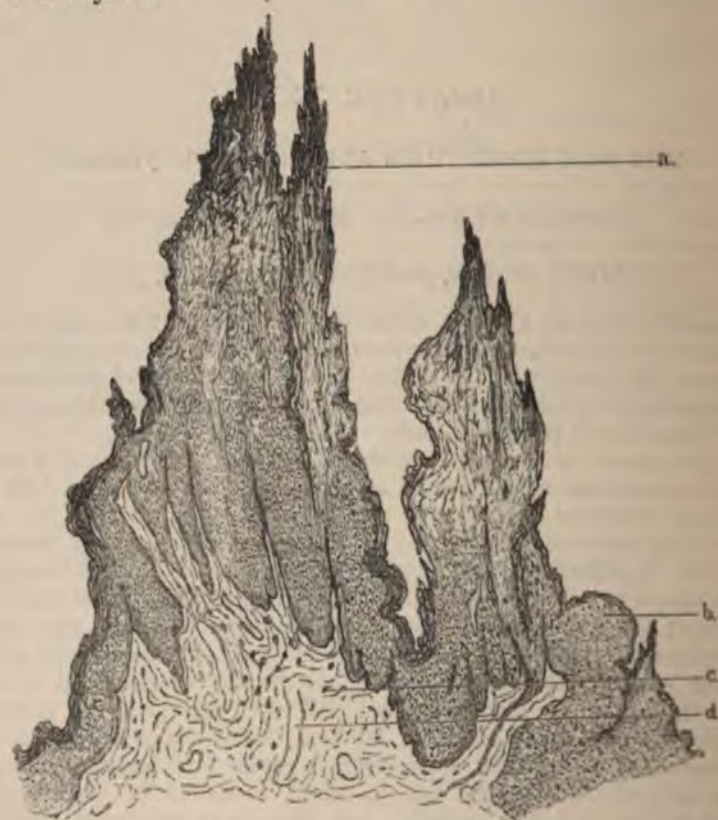


FIG. 148.—COMMON WART OF THE SKIN (×50 DIAMS.)

(*a*) Horny epidermis; (*b*) deeper more germinal part; (*c*) fibrous stroma of the centre of the wart; (*d*) blood-vessels running up into it (Picro-carmine).

(3) *V. plana.* A flat and distinctly circumscribed structure projecting but slightly from the surface of the skin.

(4) *Condylomata* and *venereal warts.*

Structure.—In the whole of the warts, the type of structure is the same, and is based upon that of a papilla, the distinctive feature between a simple papilla and a wart being essentially one of degree. The papill-

ary vessels are enlarged and dilated, the connective tissue around these vessels is also increased in quantity, while the epidermis is much thickened.

The part of the epidermis which becomes chiefly thickened in actively growing warts, such as those of venereal origin, is the rete Malpighii. In old warts, on the contrary, whose period of active growth is over, dense layers of horny epidermis accumulate on the surface, among which cell-nests may occasionally be found like those of a flat-celled cancer. Such old warts are frequently pigmented.

307. **Condylomata and Venereal Warts** have essentially the same structure, only, the epithelium is much more abundant and more actively dividing. Prickle cells are beautifully seen in some of these. *Condylomata* are due to the syphilitic poison, and grow on parts of the skin which are moist, such as the genital organs, in the axillæ, and under the mammæ. They are either flat or slightly pointed, usually present a dry surface, and, rarely, are covered by crusts. Microscopically, they are seen to be composed of an aggregation of a multitude of small papillomata.

The *venereal warts* which occur on the glans penis or other parts exposed to the discharge from a gonorrhœa or a soft chancre, have essentially the same structure, but are more filiform with a narrower base. They grow in bunches, each individual member of which contains a stem composed of a blood-vessel and a little fibrous tissue, while, around this, is a mass of germinating and highly nucleated epithelium.

Preparation.—Harden in "C" for two weeks, and subsequently for one week in "A"; stain with hæmatoxylene, or with perosmic acid and picro-carmine; mount in Farrants'.

Cutaneous Horns.

308. These may well be classified along with the papillomata. They are in reality enormously exaggerated warts with a profusion of dead epidermis on the surface.

They form conical, curved, or spiral epidermic masses, sometimes several inches in length, of a brown colour, and frequently grooved on the surface.

Fig. 149.—Section of a Cutaneous Horn in Dermatokeras (×50 Diams.)
Shows the cell-nest arrangement of the epidermis.

Microscopically they consist of a tissue like horny epidermis or nail, but sometimes there is, as in a papilloma, a central axis composed of a blood-vessel with a little fibrous tissue around it. The epidermic scales of which they are composed, sometimes have a concentric arrangement as in a cell-nest of an epithelioma, great numbers of these being seen on transverse section.

They occur chiefly on the scalp, forehead, and temples, more rarely, on the face and trunk. The author has seen a case in a boy where the whole skin was covered with them, literally from the crown of the head to the sole of the foot. This general disease is known as *dermatokeras*.

Preparation.—Harden in "A"; stain in picro-lithium carmine; mount in Farrants'.

Cancer or Carcinoma and Adenoma.

309. To perceive any resemblance to a crab (Lat., *cancer*, a crab; and Gr., *καρκίνωμα*, a malignant ulcer supposed to resemble a crab) in a cancerous tumour, would require a pretty vivid imagination. It does not much signify, however, what the term originally meant, provided that we have a clear understanding of its import at the present day. The term *epithelioma* is to be preferred for all cancerous tumours, and will be employed in the present work in this wide sense, and as synonymous with cancer.

Definition of Cancer.—*A neoplasm formed of any tissue whose fibrous interspaces and lymphatic vessels are infiltrated with actively proliferating epithelial cells.*

The sarcomata were formerly included among the cancers, and the round-celled sarcoma was called a "medullary cancer." These are now, of course, known to belong to a distinct group of mesoblastic tumours.

Many varieties of cancer were described in olden times, such as—hard, soft, epithelial, cancroid, melanotic, osteoid, villous, colloid, reticular, chondroid, hyaloid, larinoid, bunioid, encephaloid, compound, mixed, and superficial. Such subdivisions are useless and misleading. There is only *one* thing which is cancer, namely, a tumour answering to the above definition. It is immaterial whether it be hard, soft, or villous; these are minor and superficial features of the tumour.

Naked-eye Appearances of a Primary Cancerous Tumour.—(1) As a rule they are *hard* tumours. So-called soft cancers are frequently either sarcomata, or they are cancers which have suffered fatty or colloid degeneration. Of course *hard* and *soft* are relative terms, and depend for their interpretation on a general understanding as to what a hard or soft object in morbid anatomy is.

(2) They tend to infiltrate connective tissues. There is usually, as in the cancer of the mamma, a central tumour mass from which processes are seen radiating, in stellate fashion, into the surrounding parts.

(3) The border of the tumour is, as a rule, not sharply circumscribed. It is difficult to say where the tumour ends and the sound tissue commences. The connective tissue tumours, on the other hand, all have a sharp well-defined margin. They can be enucleated from the tissue in which they lie, while a primary cancer can not.

(4) They all tend to ulcerate.

(5) Cystic formation is very rare in glandular cancerous tumours, from the fact that the gland acini and ducts are destroyed in forming them.

(6) The tumour is generally single.

Naked-eye Appearances of Secondary Cancerous Tumours.—(1) They are almost always multiple. In a liver, several hundreds of such secondary cancer tumours may occasionally be found.

(2) They are usually characterised by a sharply circumscribed border. The tumour grows as a parasite in the part upon which it is engrafted. It stretches and pushes aside the neighbouring tissues, but does not tend to infiltrate them in the same manner as the primary tumour does, and hence has a sharper border.

(3) The tumours are sometimes, not always, softer than those which are primary.

Structure of Cancerous Tumours.—As stated in the definition, a cancerous tumour is a tissue infiltrated with growing epithelial cells. The kind of epithelium found in the tumour varies. All cancers spring from epithelial surfaces, and the kind of epithelium

FIG. 150.—CANCER OF THE SKIN (×350 DIAMS.)
(*a*) The epithelial cells; (*b*) the stroma enclosing them (Hæmatoxylene).

found in the tumour corresponds with that covering the surface from which it has arisen. Hence flat, spheroidal, or columnar epithelium may be found in the meshes of the growth. The old notion that there was a special cell indicative of cancer is erroneous. The only point which is typical about the cells of the tumour is that they are always epithelial; they have no constant morphological features beyond this. The true diagnostic sign is the peculiar manner in which these epithelial cells penetrate into and distend the meshes of a fibrous tissue. It is this relationship of the epithelial cells of the tumour to the stroma, which distinguishes these tumours, wherever they occur, from all others.

The accompanying figures of a cancer of the skin, of the mamma, and of the stomach show this peculiar alveolar arrangement. In the three, the cells are not of the same form. In that of the skin, they are either large flat squames, or they approach in form the cells of the rete Malpighii; in the cancer of the mamma, they resemble the small

spheroidal or cubical cells of the mammary acini; while in that from the stomach, they have the character of those from the deep part of the peptic glands. In all three cases, however, these cells lie in a fibrous alveolar mesh-work in the manner above described.

FIG. 151.—CANCER OF THE MAMMA.
(a) The epithelial cells; (b) the stroma (×450 DIAMS., Picro-carmine).

FIG. 152.—CANCER OF THE STOMACH.
(a) The epithelial cells; (b) the stroma (×300 DIAMS., Carmine).

Relation of the Stroma to the Cells.—It will be noticed, however, that the cells are not attached to the stroma. In the alveolar sarcoma a similar stroma runs through the tumour, but the cells which lie within its meshes arise from it, and are frequently found adhering to it. They are, besides, of a connective-tissue type. Such is not the case in the cancers. The cells here penetrate into the stroma as foreign bodies, they are not derived from it.

The smaller the mesh of the stroma, the denser the tumour. The cancer of the mamma is among the hardest of cancers, and the meshes in it are often so fine as to admit only a single row of cells.

The Blood-vessels.—These run in the stroma; they do not penetrate into the masses of cells contained within its meshes.

310. **Mode of Origin of Cancers in Different Parts.**—It is chiefly to Waldeyer that we are indebted for what we know of the origin of cancers. It was he who pointed out the fact that they all arise from epithelial surfaces (No. 13, xli. p. 470, and lv. p. 67).

Let us take, firstly, one of the most typical cancers, for the purpose of illustration, namely, that of the mamma; it is indicative of what occurs in the formation of all glandular cancers. The accompanying drawings (Figs. 153, 154, and 155), from a single cancerous mamma, will serve to aid the description:—

Example No. 1. **Cancer of Mamma.**—The tumour generally arises from the acini. Fig. 153 represents several normal acini lined by their polyhedral epithelium. When a cancer is about to commence growing, the epithelium within the acini begins to proliferate and distends them, as represented in Fig. 154. As yet, however, it is still confined within the acini, and thus keeps up the gland character of the growth. The tumour is as yet an **adenoma.** Not only does the epithelium distend the acini, but, within these, it sometimes rearranges itself into minor acinus-like structures, as shown in Fig. 154 (*b*, *d*). Such tumours consist of acini distended with epithelium in which secondary acini, with the epithelium circularly arranged and with a distinct lumen or channel in the centre of each, are present. They are true adenomata, and sometimes go no farther than this. The great danger, however, is that they tend to pass into the next stage and to form cancers.

FIG. 153.—DEVELOPMENT OF A CANCER OF THE MAMMA.

Acini, which may be regarded as normal (×300 DIAMS.) They are often lined with a double row of polyhedral or rounded epithelial cells.

The epithelium having distended the acinus, now ruptures through its wall, and escapes into the neighbouring fibrous stroma (Fig. 155, *b*). The stroma round the natural acini is beset with lymph-spaces (Coyne), which communicate with neighbouring net-works of lymphatics between the lobules. Into these lymph spaces the epithelium finds its way; it infiltrates them, and converts them into the alveolar fibrous meshes of the tumour. The growing epithelium acting like a foreign body, also apparently irritates the stroma and causes it to thicken; and thus the dense walls of the alveoli are formed. The tumour has now become a **cancer.** It has lost its *homologous* character, and has been converted into a *heterologous* growth.

FIG. 154.—DEVELOPMENT OF A CANCER OF THE MAMMA. LOBULE OF THE GLAND IN WHICH THE ACINI ARE IN THE ADENOMATOUS STAGE (×50 Diams.)

(*a*) Normal acinus; (*b*, *d*) acini distended with epithelium; (*c*) surrounding stroma.

FIG. 155.—DEVELOPMENT OF A CANCER OF THE MAMMA. A SET OF ADENOMATOUS ACINI BECOMING CANCEROUS (×350 DIAMS.)

(*a*) An adenomatous swelling of an acinus; (*b*) the cells of a similar swelling which have broken out, and are invading the surrounding stroma; (*c*) part which is cancerous (Hæmatoxylene and eosin).

Example No. 2. **Cancer of a Salivary Gland.**—When a salivary

FIG. 156.—ADENOMATOUS STAGE OF A CANCER OF THE SUBMAXILLARY GLAND (×350 DIAMS.)

(*a*) Section of a normal acinus; (*b*) an acinus distended with proliferating epithelium. Other parts of the gland were completely cancerous (Carmine).

gland, such as the submaxillary, becomes cancerous the tumour passes

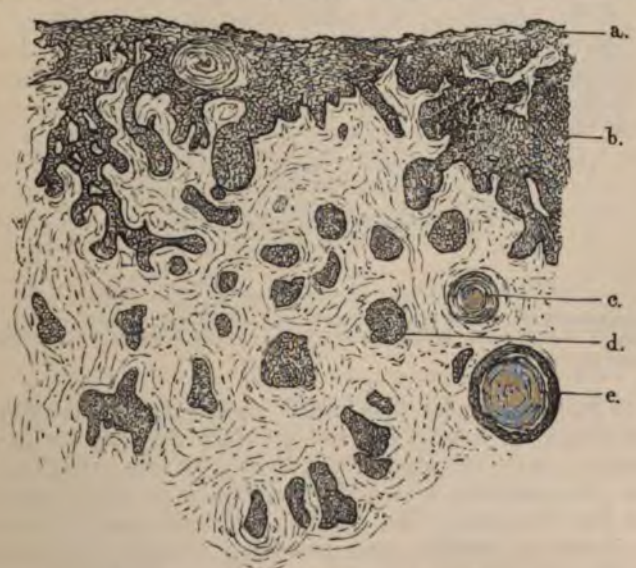


FIG. 157.—CANCER OF SKIN (×50 DIAMS.)

(*a*) Horny layer not much altered; (*b*) irregularly club-shaped processes projecting downwards from the rete Malpighii; (*c*, *e*) cell nests; (*d*) an alveolus filled with epithelium (Perosmic acid and picro-carmine).

through the same adenomatous stage as in the cancer of the mamma. The large pyramidal epithelial cells which naturally line the acini begin to proliferate with inordinately great activity; and the acinus becomes filled with them, and ultimately distended. The cells also lose their characteristic shape and become smaller. In course of time they burst into the stroma and infiltrate its meshes, thus constituting a cancer.

Example No. 3. **Cancer of the Skin.**—In a young cancer of the skin the first noticeable alteration is, that the cells in the rete Malpighii

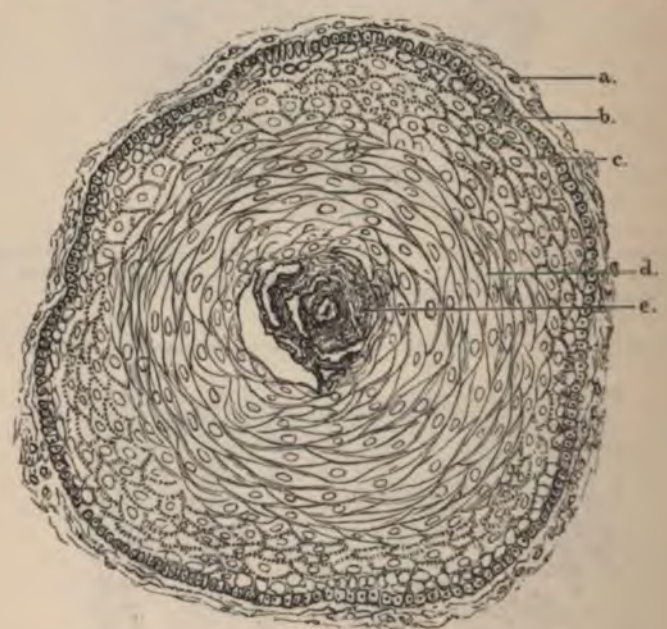


FIG. 158.—A CELL NEST FROM A CANCER OF THE LIP (×300 DIAMS.)

(*a*) The stroma of the alveolus in which the cell nest is contained; (*b*) small germinal cells of the periphery; (*c*) prickle cells; (*d*) compressed squames; (*e*) degenerated cells in the centre (Perosmic acid and picro-carmine).

begin to proliferate more than usual. Large, obtuse, club-shaped or pointed masses of new, young, and growing epidermis are projected downwards into the subjacent derma, and thence into the subcutaneous tissues. The condition is thus identical with a glandular cancer such as that just described. The growing epidermis gets into the wrong place. Instead of covering and protecting connective tissue surfaces, as it ought to do, it pierces into them and distends their interfibrillar spaces. Having invaded them, it continues growing, and converts them into large alveolar cavities. In the centre of these masses of epithelium a concentric arrangement of the epithelium is frequently

seen, constituting what is known as a **cell nest**. At other times the whole alveolus may be occupied by the cell nest. The property of infiltrating a neighbouring fibrous stroma is, therefore, practically the same here as in the mamma, the only point of difference being as regards the character of the cells.

Literature on Adenoma.—Consult literature of various organs, and :—**Balzer** (Sebaceous A. of Face) : Arch. d. Physiol. norm. et path., vi. 1885, p. 564. **Bock** (Sebaceous Glands) : Arch. f. path. Anat., lxxxi. 1880, p. 503. **Loeb and Arnold** (Pituitary Body) : Arch. f. path. Anat., lvii. 1873, p. 172. **Willigk** (Liver) : Arch. f. path. Anat., li. 1870, p. 208.

311. **Lymphatic Infection.**—The cause of the secondary infection of the lymph vessels, which so readily occurs in cancers, is evident when their origin is understood. The lymph spaces into which the epithelium burrows, are, in reality, the radicles of the larger lymph vessels, and hence the cells of the tumour which are contained in them are directly conveyed to the lymphatic trunks with which they are in communication, and by these again to the lymphatic glands.

It is said that the infection of the lymphatics does not occur so frequently in the sarcomata as in the cancers. This may be accounted for by the fact that, as the sarcoma grows, it destroys all the lymph spaces in its neighbourhood.

Cysts are not usual in cancers of tubular glands, and the reason is apparent. The gland structures, by whose dilatation the cysts would be constituted, are destroyed, and hence nothing remains in the tumour to form a cyst.

The secondary tumours are accounted for by some of the cells of the primary tumour having been carried into the organ by the blood or lymph channels. As might be expected, the variety of epithelium within them is identical with that of the primary tumour.

312. **Malignancy of Cancers.**—They are all malignant; but, with the exception of the cancer of the mamma, are probably not so much so as the sarcomata. The flat-celled cancer of the skin or of a mucous membrane is an easily-eradicated tumour if treated early enough. The cause of its being less malignant than that of the mamma is probably that its cells are larger, and consequently, not so easily transported.

It has often been alleged that cancerous growths are contagious. Of late, Scheuerlen (for refs. see bibliog.) has isolated from cancers of the mamma a **bacillus** which he asserts is the active agent in their causation. It grows readily on blood-serum, agar, and gelatine, slowest upon the last; and forms a red deposit on potato. Its spores stain only by the Ehrlich method in use for the tubercle bacillus, but the bacillus itself stains readily enough by ordinary means. The bacillus is from 0·15 μ long and 0·5 μ broad; while the spores are 1·5 μ long and 0·8 μ broad. He has injected pure cultures into the mammary glands of bitches, with the effect of inducing a hard tumour which, he states, is epithelial in its nature.

Koch and the other Berlin bacteriologists are inclined to doubt its having to do with **cancer**, and look upon the morbid condition of the mamma set up as being simply a **mastitis**.

313. **Degenerations.**—These are chiefly (1) the *fatty* and (2) the *colloid*. Cancers of the alimentary canal are specially prone to become colloid. The cells degenerate into a clear homogeneous jelly-like substance, while the stroma is left dissected out. (3) The *mucoid degeneration* is much rarer in cancers than in tumours of the connective-tissue type. It is said to affect the stroma of the tumour, and to leave the cells uninjured.[1] (4) They are all liable to *ulcerate* and subsequently to *granulate*, and when in this latter condition, may be mistaken for ordinary fungating ulcers. They prove quite intractable to treatment, however; and if the surface of the granulations be lightly scraped, the epithelial character of the cells removed, as well as the occasional presence of cell nests, sufficiently attest the nature of the growth. The granulations in such cancerous ulcers are long and flabby, and are filled with cell nests and granulation cells.

314. **Melanotic Cancer (?).**—As previously stated (Sect. 137), it is questionable whether the epithelial cells of a cancerous tumour ever take on a true melanine forming property.

Preparation.—This depends on the organ or tissue in which the cancer is situated. If in a gland, harden in "A," stain in hæmatoxylene, and mount in Farrants'. If in the skin or in a mucous membrane, harden in "A," stain in hæmatoxylene, clarify with saturated solution of picric acid in methylated spirit, followed by ¼ per cent solution of eosin in methylated spirit, and oil of cloves. Mount in dammar.

Rodent Ulcer.

315. This was described by Thiersch (No. 37) as a flat or superficial epithelioma, and there seems little doubt that it is of an epitheliomatous nature. It commences as a soft tubercle, usually situated upon the face, covered by smooth skin, and somewhat resembling a wart. If incised, the interior is found to be filled with a brownish-coloured pultaceous material. The wart-like mass may remain on the face unaltered for years, but, in course of time, has a tendency to ulcerate. The ulcer spreads slowly but constantly, and if left alone may destroy the bones of the face or the whole cheek. It may ultimately prove fatal. It does not tend to affect neighbouring glands (Sir B. C. Brodie. See Paget, No. 23).

Characters of the Ulcer.—It is irregular in shape, but has a general tendency to be round or oval. The base is smooth, not warty or nodular, and may even be granulating. It is comparatively dry and glossy, has a scooped-out appearance, and yields little discharge. The border is slightly elevated, not undermined, but smoothly rounded or slightly nodular.

Microscopically it presents most of the characters of an epithelioma; but differs from an ordinary epithelioma of the skin in the following particulars:—

[1] Consult Malassez, No. 4, January, February and March 1883.

(1) The cells are smaller and more rounded.

(2) The cell nests, although undoubtedly present, are less abundant.

(3) The epithelial processes are very angular and branching.

(4) They are sharply constricted at parts, and are wide at others.

(5) They do not tend to burrow deeply, but rather to spread superficially under the sound epidermis. The edge of the ulcer usually contains a great many of these processes.

(6) There is an absence of the club-shaped masses of sprouting epidermis derived from the rete Malpighii.

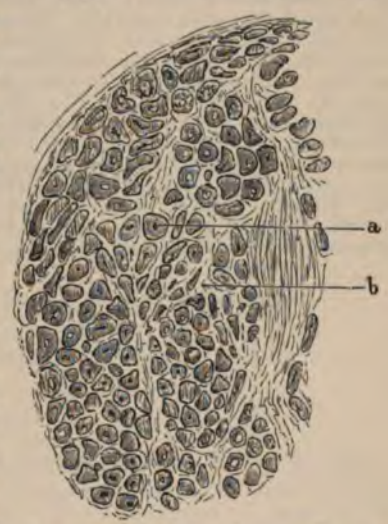


FIG. 159.—ADENOMATOUS STAGE IN FORMATION OF A RODENT ULCER (×50 DIAMS.)
(*a*) Adenomatous (sweat) gland acini; (*b*) the stroma (Picro-carmine).

Point of Origin.—It evidently does not arise from the epidermis, but more likely from the sweat (Thin) or sebaceous glands. If the nodular mass which precedes the ulcerated stage be examined microscopically, it will be found to be a typical adenoma (see Fig. 159). The acini are small, but very numerous, and the majority of them still possess a channel in the centre. There is a tendency for these gland, acinus-like, structures to fuse together into a uniform mass, which in course of time ulcerates out, and leaves the smooth floor of the ulcer, while, at the edge, the glandular epithelium continues to grow and spread underneath the sound skin. The character of the acini in the adenomatous stage points to their origin from the glands of the skin, most probably from the sweat glands.

The cause of the ulcer spreading superficially is not known.

Preparation.—As for cancers.

Literature on Carcinoma.—Consult lit. of various organs, and:—**Alberts:** Das Carcinom, etc., 1887. **Ball** (Paraffin C.): Lancet, 1885, i. p. 1037. **Ballance** (Cultivation Experiments): Trans. Path. Soc. Lond., xxxviii. 1887, p. 412. **Baumgarten** (on Scheurlen's C. Bacillus): Centralbl. f. Bakteriol. u. Parasitenk., iii. 1888, p. 397. **Brault** (non-Bacterial Origin): Arch. gén. de Méd., 1885, ii. pp. 458, 586. **Brüggemann:** Ueb. d. Entwickelung. d. Cancroids a. gutartigen Hautgeschwülsten, 1885. **Budd** (Question of Contagiosity): Lancet, 1887, ii. p. 1091. **Butlin** (Report on C. of Breast): Brit. Med. Journ., 1887, i. p. 436. **Coats** (C. in Certain of its Path. Aspects): Glasg. Med. Journ., xxv. 1886, p. 249. **Gross** (Two Hundred Cases): Med. News, Phila., li. 1887, p. 613. **Hauser** (Cylinder-cell C.): München med. Wochnschr., xxxv. 1888, p. 198. **Hutchinson** (Scirrhus following Adenomena of Breast): Brit. Med. Journ., 1887, ii. p. 1280. **Eckardt:** Vier neue Fälle v. Paraffin-Krebs, 1886. **Erbe:** Ueb. d. Entwick. secundärer C. durch Implantation, 1884. **Francke** (Diagnosis and Etiology of Sarcoma and C.): München med. Wochnschr., xxxv. 1888, p. 57. **Kirmisson** (Microbic Nature of C.): Bull. méd., ii. 1888, p. 567. **Ledoux-Lebard** (C. a Parasitical

Disease): Arch. gén. de méd., 1885, i. p. 413. **Macewen** (C. in its Path. and Etiol. Aspects, etc.): Glasg. Med. Journ., xxv. 1886, p. 271. **Malherbe** (Classification): Arch. gén. de Méd., 1885, ii. pp. 513, 656. **van Nüss**: Beitrag z. Enstehung d. Carcinome aus chronisch-entzündlichen Zuständen d. Hautdecken, 1886. **Paget**: Cancer and Cancerous Diseases, 1887. **Pfeiffer** (Scheurlen's Bacillus a Saprophyte): Deut. med. Wochnschr., xiv. 1888, p. 203. **Pinner**: Die Krebskrankheit, Ursachen, etc. 1888. **Rappin** (Microbe of): Compt. rend. Soc. d. Biol., iv. 1887, p. 756. **Savory**: Brit. Med. Journ., 1884, ii. p. 1173. **Scheuerlen** (Etiology): Deut. med. Wochnschr., xiii. 1887, p. 1033; *also*, Berl. klin. Wochnschr., xxiv. 1887, p. 935; *also*, Allg. med. Centr. Ztg., lvi. 1887, p. 1729. **Schill** (Bacilli in): Deut. med. Wochnschr., xiii. 1887, p. 1034. **Schuchardt** (Origin fr. Old Inflammatory Condition): Samml. klin. Vortr., 1885, No. 257 (Chir., No. 80, 2195); *also*, Beiträge z. Entstehung d. Carcinome aus chronischen entzündlichen Zuständen, etc. 1885. **Senger** (Etiology): Berl. klin. Wochnschr., xxv. 1888, p. 185. **Trost**: Beiträge zur Frage ub. d. Uebertragbarkeit d. Carcinome, 1887. **Virchow** (Diagnosis and Prognosis): Arch. f. path. Anat., cxi. 1888, p. 1; *also* (transl.), Lancet, 1888, i. pp. 145, 179; Arch. f. path. Anat., i. 1847, p. 94. **Williams (W.R.)**, [Family History]: Brit. Med. Journ., 1884, i. p. 1039; *also*, Lancet, 1886, i. p. 146. **Williams**: An Introduction to the Path. of C. and Tumour Formation, on the Basis of Evolution, 1886.

CHAPTER XXVIII

THE NEW FORMATIONS AND TUMOURS—(*Continued*)

ANOMALOUS TUMOURS DUE TO VARIOUS CAUSES

POLYPI AND CYSTS

POLYPI.

316. **Definition.**—*Any pyriform, pendulous, and pedunculated tumour growing from a mucous membrane.* They have no constant structure, but are composed of all kinds of tissue. The commonest of these are the fibrous, muscular, and sarcomatous. Cancers occasionally become pendulous when situated on a mucous membrane, but rarely.

Sites.—The commonest are the cavities of the nose, ear, uterus, stomach, œsophagus, and intestine. Of all parts of the alimentary canal the rectum is perhaps the most usual situation.

Mucous Polypus.—This is the variety which is commonest, and is particularly a tumour of the nares, the external auditory meatus, and the uterus. It gets its name from the soft, velvety, mucous-membrane-like consistence which it possesses. It has a pink colour, and is frequently attached by a long pedicle.

Microscopically, it is composed of an open areolar fibrous tissue, whose meshes are distended with œdematous fluid. So œdematous is it, that if laid upon an absorbent surface the tumour shrivels into a mere shred of tissue within a short time. Lying upon the walls of the meshes are numerous round cells—probably young fibroblasts—and groups of these are occasionally seen at certain parts of the tumour. The surface is covered by the particular variety of epithelium which naturally invests the mucous membrane from which the tumour has arisen.

Mucous glands are occasionally dragged into it, and may become cystic. Those of the uterus are often converted into cysts of large size. From the fact that these tumours contain mucous glands more or less altered, they have sometimes been classified as adenomas. This, however, is erroneous. The fact that they contain glands is purely

an accident due to their situation, just as a sarcoma or fibrous tumour of the mamma contains glands because it grows in the midst of a glandular structure.

Mode of Formation.—The mucous polypus is nothing more, originally, than a fibrous tumour of a mucous membrane. Let A

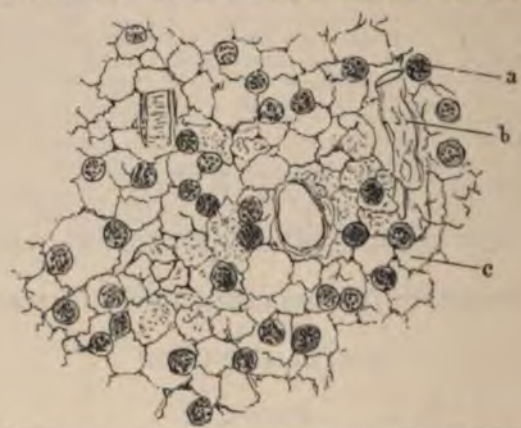


FIG. 160.—TISSUE COMPOSING A MUCOUS POLYPUS OF THE NOSE (×400 DIAMS.)
(a) Young fibroblasts; (b) a blood-vessel; (c) the œdematous areolar spaces (Hæmatoxylene).

(Fig. 161) represent the tumour in its commencement. It originates in the fibrous tissue of the mucous membrane, and as it increases in size, grows in the direction of least resistance, namely, into the cavity which the mucous membrane lines. It pushes the epithelium in front

FIG. 161.—SCHEME OF FORMATION OF A POLYPUS.
A, First stage; B, second; C, third. (a) artery entering, and (v) vein leaving the tumour; (e) epithelium; (t) tumour substance.

of it, and insinuates itself between the glands of the membrane. By virtue of its weight it drags upon its attachments and forms for itself a pedicle (B). An artery or several arteries (*a*) enter it, and venous channels (*v*) return the blood from it. As the blood has to return against gravity and has to pass through the narrow pedicle, it experiences some obstruction to its onward course. Hence the tumour becomes

œdematous, and the more attenuated the pedicle, the more is this tendency to œdema encouraged (C). The fibrous tissue of the original tumour thus becomes opened out and converted into the reticular tissue of the tumour. The mucous glands are surrounded by the tumour, and their mouths are frequently obstructed, so that secretion accumulates within them; they become retention cysts. The vessels within the tumour are often varicose and very numerous, so that they may bleed profusely when injured.

Dense Fibrous Polypi.—Fibrous polypi, occasionally, are dense and hard, as when found growing into the pharynx from the posterior nares. The pedicle in these cases is broad, so as not to obstruct the blood return.

Muscular Polypi.—These are chiefly found attached to the

FIG. 162.—POLYPUS OF RECTUM SHOWING THE GLANDS OF THE TUMOUR (×350 DIAMS.)
(*a*) Gland lined by columnar epithelium; (*b*) stroma of the tumour (Picro-carmine).

uterus. They are in fact small myomata; or they may be small fibrous tumours of the mucous membrane of the uterus into which some of the muscular fibres of the uterus have been dragged.

Sarcomatous Polypi are also found growing from the uterine mucous membrane. They are malignant, as might be expected from their nature.

Channel Polypus.—This was the name given by Oldham to a polypus of the cervix uteri, which is pierced from the surface inwards by numbers of channel-like openings usually containing mucus. The channels are sometimes so capacious that a crow-quill can be passed up into them. In such tumours several cysts are also usually seen projecting on the surface and distended with mucus.

The channels are lined by beautiful columnar epithelium; and it is

evident that they are simply the uterine glands distended from some cause. The most evident explanation of their formation seems to be, that the retention cysts, which are so constantly seen contemporaneously with the channels in these tumours, become over distended with mucus, and rupture. The opening cicatrises and remains patent, mucus being constantly discharged from it. The ruptured cyst now becomes elongated and constitutes the channel.

FIG. 163.—CHANNEL POLYPUS OF CERVIX UTERI (×50 DIAMS.)
(*a*) Fibro-cellular stroma of tumour; (*b*) a gland of uterine mucous membrane; (*c*) a channel; (*d*) lining of columnar epithelium (Carmine).

Preparation.—If very soft, harden in "C" or "D"; if denser, in "A"; stain in carmine or hæmatoxylene, the latter either followed or not by eosin; mount in Farrants'.

CYSTS.

317. **Definition.**—*A cyst is a hollow tumour whose wall is formed by a continuous membrane covered by epi- or endothelium, and whose cavity is filled with fluid, semi-fluid, or solid contents, excreted or secreted by the membrane.*

No class of bodies in pathology is so loosely defined as that of cysts. Any sort of a cavity is called a cyst, and consequently, the greatest confusion prevails as to what is a cyst and what is not.

Is a hæmorrhage which becomes surrounded by fibrous tissue, a cyst? Certainly not; that is to say, it cannot be classified in the same category, as the slightest reflection will prove, with the cystic distension of a urinous tubule or of a mammary acinus. It is an *encapsuled hæmorrhage*. If a solid foreign body became surrounded by fibrous tissue, the capsule might also be called a cyst with equally good show of reason.

Is a hæmatocele a cyst? Here we have to do with a shut sac, a distinct membrane, and a fluid poured out from that membrane. The membrane, moreover, is lined by endothelium. This must, therefore, be classified as a true cyst.

Is a hæmorrhage into the abdomen then a cyst? It is so if the hæmorrhage is localised and forms a tumour.

Parts which suffer from mucous degeneration frequently show

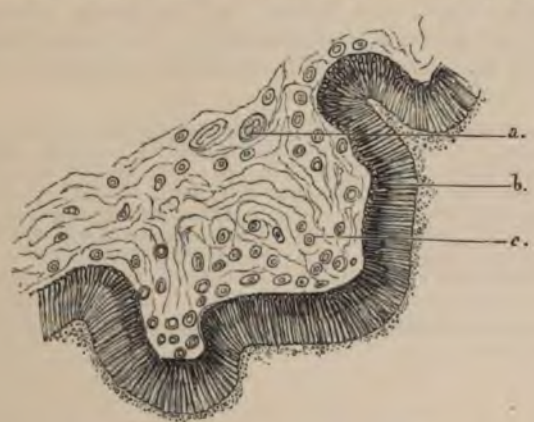


FIG. 164.—WALL OF A CYST IN A POLYPUS OF THE CERVIX UTERI (×300 DIAMS.)
(*a*) A small artery; (*b*) epithelium lining the wall; (*c*) connective-tissue cells of the wall (Carmine).

little angular cavities filled with mucin-holding fluid—Are these cysts? They cannot be so called, for they have no lining membrane, no endothelium, and the contents are the result simply of a degeneration of the tumour. These are *myxomatous cavities*, not cysts.

Formation of Cysts.—All true cysts originate in pre-existing hollow structures. These are most commonly the ducts and acini of glands, such as those of the mamma, or they may be lymphatics. The name "retention cysts" is sometimes employed to designate those formed from gland tubes. This seems to be needless, as all true cysts in reality originate in a retention of the products of some gland, channel, or cavity.

There is only one apparent exception to this rule, namely, the **hydatid cyst**, which is of so special a nature that it can hardly be classified as a cyst at all. It is a parasite whose natural state, when lying in the tissues, is to become distended with fluid secreted from its

membranes. The cyst, in this case, has not a retention character, but is the result of a hollowing out of the body of the embryo parasite.[1]

Classification of Cysts.—It is very difficult to classify them in a scientific manner, owing to their being due to so many causes, and consequently, the only one which shall be here attempted is into *simple* and *compound*, according as the tumour is constructed of a single cavity or of several.

A simple cyst is one having a single cavity filled with various contents. A compound cyst is one composed of several cavities which may grow one within the other. The secondary and tertiary cysts sometimes spring from the walls of the primary by endogenous development. Such are called *proliferous cysts*; but at other times the individual cavities remain separate, and when so, are usually designated *multilocular cysts*.

Contents.—These are various, such as serum, mucus, colloid, blood, sebaceous secretion, or cholesterine. The walls of those found in the ovary and subcutaneously sometimes contain hair and skin (*dermoid*), or teeth.

Literature on Anomalous Tumours.—Consult literature of various organs, and:—**Aussenac**: Contribution à l' Étude des Kystes du Maxillaire inférieur, 1885. **Bayer** (Transformation of muc. Polypi into Malignant Tumours): Deut. med. Wochnschr. xiii. 1887, p. 174. **Chapin**: Two cases of Branchial Cyst, 1885. **Cusset** (Branchial Cysts): Cong. franc. de Chir. Proc.—verb., 1887, ii. p. 553. **Grawitz** (Dermoid-like Cysts on Peritoneum): Arch. f. path. Anat., c. 1885, p. 262. **Masse** (Origin of Dermoid Cysts): Bull. gén. de Thérap., cviii. 1885, p. 337. **Senn**: On Branchial Cysts of Neck, 1884. **Treves** (Malignant Cysts of Neck): Trans. Path. Soc. Lond., xxxviii. 1887, p. 360.

[1] For examples of the formation of special cysts, consult chapters on diseases of the mamma, kidney, etc.

CHAPTER XXIX

THE NEW FORMATIONS AND TUMOURS—(*Continued*)

TUMOURS DUE TO THE PRESENCE OF A SPECIFIC VEGETABLE MICRO-ORGANISM.

TUBERCLE, LUPUS, GUMMA, ETC.

TUBERCLE.

318. *Historical.*—It would be quite beyond the range of this work to give anything like a complete history of the subject of tubercle, and, accordingly, a synopsis, necessarily brief, of the most prominent doctrines which have been entertained regarding its nature from Laennec's time downwards, will alone be attempted.

Laennec's Views.—In former times, all caseous deposits were called tubercles by Laennec (No. 38, 1834), and of these he described four varieties :—(1) *Miliary*[1] *tubercle*, where the tubercles are the size of a millet seed, of a gray colour, and usually arranged in groups. (2) *Crude tubercle*, where the miliary nodules run together into masses and become yellow. (3) *Granular tubercle*, where the nodules are extremely small, nearly the size of a millet seed, and scattered uniformly through a whole organ. They are not arranged in groups, and have no tendency to run together. Centrally they become transformed into yellow tubercle. Bayle (No. 39) considered them to be portions of cartilage on account of their hardness. (4) *Encysted tubercles*, or such as are constituted of a hard mass of crude tubercle in the centre, with a fibrous-like or semi-cartilaginous capsule outside.

Virchow's Classification.—A few years after this, Virchow (No. 35) showed that the so-called tubercles of Laennec varied in structure and mode of origin. Thus he found some of them to be little connective-tissue deposits, while he demonstrated that others, such as t "crude tubercle" of the lung, were pneumonic accumulations wh had caseated. He consequently called the disease of the lung acc

[1] *Milium*, a millet seed.

panied by crude tubercle, "caseous catarrhal pneumonia," while he reserved the name *tubercle* for bodies like those seen in a general acute eruption.

Villemin's Discoveries.—In the year 1865 Villemin (No. 40, lxi. p. 1012), showed that in rabbits an eruption of miliary nodules, in all respects similar in their general characters to so-called miliary tubercle in Man, could be induced within a few weeks by the inoculation of cheesy deposits in different parts of the body. The cheesy material evidently contained something which, on being absorbed, had the power of spreading tuberculosis broadcast.

Sanderson's Experiments.—Sanderson (No. 41, 1868-69), confirmed these experiments, but further showed that the mere presence subcutaneously of a foreign body, such as a seton, is sufficient to set up an eruption of tubercle in the lung in guinea-pigs within a few weeks of its introduction.

Cohnheim's Test.—The question of the nature of tubercle lay in a very troubled and uncertain condition for several years after this, and there was a tendency during this time to fall back upon histological structure as the true distinctive feature of what was tubercular and what was not. In the year 1880, however, Cohnheim (No. 42) asserted that the only test of a deposit being tubercular was its inoculability. "All is tubercular," said he, "which by transference to properly constituted animals is capable of inducing tuberculosis, and nothing is tubercular unless it has this capability."

Koch's Discoveries.—Finally, in the year 1882, Koch's famous paper appeared (No. 43, April 10, 1882), in which he announced that he had found a specific bacillus in tubercular deposits, which had characteristic morphological features, which gave a peculiar reaction with certain aniline dyes, which could be cultivated artificially, and which when inoculated was capable of exciting a tubercular eruption; while, in the nodules of the eruption, the organism was again to be found. He defined tubercle as any growth of newly-formed tissue which contains the tubercle bacillus, quite irrespective of situation, histological structure, or distribution.

Literature on Tubercle—Historical.—Consult literature given under tubercle of various organs, and :—**Baillie :** Morbid Anatomy, p. 41, 1833. **Baumgarten :** Ueb. Tuberkel u. Tuberkulose, 1885. **Bayle :** Rech. sur la phthisie pulm., 1810. **Bennett :** Path. and Treat. of Pulm. Tubercul., 1853. **Billings :** J. Comp. Med. and Sur., N. York, vii. 1885, p. 62. **Bollinger :** Zur Aetiologie d. Tuberculose, 1883. **Carswell :** Path. Anat., 1838. **Cornille :** De la contagiosité de la tuberculose, 1882. **Discussion** on Tubercle : Tr. Intern. M. Cong., i. 1881, p. 303. **Eichstaedt :** Die Tuberculose, 1884. **Gee :** "Tuberculosis," Quain's Dict. of Med., 1882. **Grancher :** Tribune Méd., xiv. 1881. **Graves :** Clinical Lectures, Dublin, 1837-48. **Klebs :** Arch. f. path. Anat., xliv. 1868, p. 242. **Klein :** Practitioner, xvii. 1881, p. 81. **Landouzy and H. Martin :** Rev. d. Méd., iii. 1883. **Lombard :** Essai sur les Tubercles, 1827. **Louis :** Rech. anat.-path., 1842. **Niemeyer :** Lectures on Phthisis (transl.), New. Syd. Soc. **Reinhardt :** Ann. d. Berlin. Char., i. 1850, p. 362. **Rindfleisch :** Cycl. Pract. Med., v. Ziemssen (transl.), v. 1875, p. 633. **Science (Koch's** Work). Cambridge, iv. 1884. **Shattuck :** Cycl. Pract. Med., v. Ziemssen, 1881 ; suppl. vol. p. 334. **Spina :** History of Tuberculosis (transl.), 1883. **Virchow :** Würzb. Verh., i. 1850, p. 80 ; *Ibid.*, ii. pp. 24 and 70 ; *Ibid.*, iii. p. 98.

CHARACTERS OF THE TUBERCLE BACILLUS.

319. It varies considerably in length but is generally from a quarter to half the breadth of a coloured blood corpuscle ($\frac{1}{7500}$ in). It may, however, equal it or be even longer. It is usually considerably longer when found in the sputum than it is when occurring in the tissues. It is narrow, more or less rounded at the ends, and generally has a beaded appearance owing to its containing spores. The number of spores in a single rod varies from four to eight, but is on an average six. The bacilli lie either singly, in pairs (the one superjacent to the other), in groups of seven, ten, or more, or in rosette-like masses. They are either straight, or have a slight curve, often towards one extremity. When cultivated, they become, as a rule, shorter.

(For further particulars see Vol. II., "Vegetable Parasites.")

TISSUES IN WHICH THE BACILLUS IS FOUND.

320. As a general statement, it may be said, that in cases of tuberculosis, acute or chronic, the bacillus will be found lying in *some* of the nodules. There is this peculiarity, however, about its distribution, namely, that it is very irregular. The author has met with a case in which both lungs were rendered perfectly solid from an extremely acute eruption of tubercle, but in which not a vestige of any tubercle bacillus could be discovered after the most careful and prolonged examination. The tubercular nature of the disease was confirmed, or at any rate supported, by there being similar nodules in other organs. A remarkable fact was that none of the nodules in the lung had caseated. They were all as yet in the cellular stage, but presented the histological features of acute tubercle. It is usually where **caseous catarrhal pneumonic** or **interstitial tubercle nodules** have *caseated* and are *in process of disintegration* that the largest deposits are to be seen; but even in lungs in this condition it is sometimes impossible to demonstrate it with anything like the constancy that might be expected. The explanation that is usually given to account for its absence in so many nodules which are undoubtedly tubercular, is that it has worked itself out in them, and that the tumour which is left is merely its effect.

Fütterer (No. 13, c. p. 236), describes them as lying in **a blood-vessel** in the neighbourhood of a miliary tubercle; **around a vessel** in the centre of a tubercle; in the **vasa afferentia** and **efferentia** of the glomeruli of the kidney; in the **Malpighian body** of the kidney; and in a **convoluted urinary tube.** Benda (No. 43, No. xii. 1884), has seen them within **thrombi** of veins lying in the neighbourhood of a large cheesy collection in the kidney, as well as in the glomeruli. A tubercular eruption containing the bacillus has also been recorded by Weigert within the larger branches of the **pulmonary artery** (No. 13, civ. p. 31, 1886). They were somet

scattered broadcast over the tunica intima, at others were confined to particular localities. Herxheimer (No. 13, cvii. p. 180, 1887), has described a similar case. In a case of miliary tuberculosis in a child, the author has seen a tubercular growth so large as nearly to obliterate a middle-sized branch of the pulmonary artery.

Muhlert (No. 151) in investigating thirty cases of tuberculosis found the bacillus present with few exceptions in the tubercles of the brain-membranes, the choroid plexus, brain substance, lungs, air-passages, tonsils, spleen, liver, kidneys, intestine, peritoneum, bone-marrow, granulations, lymph-glands, etc.

It is, therefore, beyond question that the bacillus is freely transported by the circulating blood throughout the different organs. Wherever it alights, it occasions the growth of a tubercle nodule.

In **gelatinous degeneration** and in old sinuses of joints it has been found connected with tubercles present in these diseased conditions. In the tubercular **human mamma** and in the **tubercular udder** of the cow it is abundant, while from the latter it is thrown off in large quantity into the milk.

Literature on Tubercle Bacillus.—**Babes** (Tubercle and Lepra B.): Compt. rend. Acad. d. Sc., xcvi. 1883, pp. 1246-1323; (In Urine): Centralbl. f. d. med. Wissensch., xxi. 1883, p. 145. **Balmer and Fraentzel:** Berl. klin. Wochnschr., xix. 1882, p. 679. **Barron:** Liverp. Med. Chir. Journ., iii. 1883. **Baumgarten:** Centralbl. f. d. med. Wissensch., xxi. 1882, p. 337; *Ibid.*, xx. 1882; and v. 1884; Deut. med. Wochnschr., viii. 1882; *Ibid.*, ix. 1883. **Carreras-Solá:** Rev. de cien. méd., Barcel., xi. 1885, p. 201. **Cheyne:** Brit. Med. Journ., 1885, i. p. 169. **Chiari:** Oestere. ärztl. Vereinzeitung., vii. 1883. **Demme** (Diagnostic Value): Berl. klin. Wochnschr., xx. 1883. **Discussion on:** Verhandl. d. Cong. f. innere Med., Wiesbaden, ii. 1883. **Discussion on:** Lancet, 1883, i. p. 234. **Discussion:** Lancet, 1885, i. pp. 107-155. **Dreschfeld** (Diagnostic Value): Brit. Med. Journ., 1883, i. p. 304. **Ernst:** Boston M. and S. Journ., cix. 1883. **Flint:** Med. News Phila., xliv. 1884, p. 60. **Formad:** Phil. Med. Times, 1882, 1883-4; N. Y. Med. Journ., xxxix. 1884. **Fulton** (B. Cause or Effect of Tuberculosis?): Kansas City Med. Rec., i. 1884, p. 370. **Gaffky** (Sputum): Mittheil. a. d. k. Gesundheitsamte, ii. 1884, p. 126. **Graham:** Canada Practitioner, Toronto, viii. 1883. **Green:** Brit. Med. Journ., i. 1883, p. 193. **Hagueny:** Du Bacille de la Tuberculose, 1883. **Handford** (Review): Lancet, 1885, ii. pp. 988-1038. **Heron:** Lancet, 1883, i. pp. 38, 188. **Kidd:** Proc. Roy. Med. and Chir. Soc. Lond., i. 1882-85, p. 301; Brit. Med. Journ., 1884, ii. p. 1193. **Kirstein** (In Urine): Deut. med. Wochnschr., xii. 1886, p. 249. **Koch:** Berl. klin., Wochnschr., xix. 1882, p. 221; *also*, Deut. med. Wochnschr., ix. 1883; *also*, Allg. Wien med. Ztg., xxviii. 1883; *also*, Mitth. a. d. Gesundheitsamte, ii. 1884, p. 1; *also*, Arch. f. Physiol., 1882, p. 190; *also*, Med. Chir. Centralbl., Wien, xvii. 1882; *also*, *Ibid.*, Wien, xix. 1884, p. 50. **Lindner** (In Joints): Jahrb. f. Kinderheilk, Leip., xxi. 1884, p. 136. **Lustig** (In Blood): Wien. med. Wochnschr., xxxiv. 1884, p. 1429. **Mackenzie:** Edin. Med. Journ., xxix. 1883-84, ii. p. 681. **Menard** (Connection of Abscesses with Tuberculosis): Bremer Weekly Med. Rec., Chicago, ix. 1884. **Mendelsohn** (In Urine): Deut. med. Wochnschr., x. 1884, p. 7. **Meisels** (In Blood): Wien. med. Wochnschr., xxxiv. 1884, p. 1149. **Muhlert:** Beitr. zur Kentniss üb. d. Vorkommen d. Tub. Bacillen, 1885. **Pfeiffer** (Sputum): Berl. klin. Wochnschr., xx. 1883, p. 32. **Pilatte:** Recherches expérimentales sur le Bacille de la Tuberculose, 1885. **Prudden** (Tubercle in which Bacillus not demonstrable by ordinary method of Staining): N. Y. Med. Rec., xxiii. 1883. **Rutimeyer:** Centralbl. f. klin. Med., vi. 1885, p. 353. **Sauvage:** De la Valeur diagnostique de la Presence des Bacilles de Koch dans les Crachats, 1883. **Schill** (Sputum): Deut. med. Wochnschr., ix. 1883. **Schmidt:** Chicago Med. Journ. and Examiner, xlv. 1882; *also* (Pseudo-bacillus Tuberculosis): Chicago Med. Journ. and Examiner, xlvi. 1883. **Schottelius** (Critique): Arch. f. path. Anat., xci. 1883, p. 129. **Sée** (Transl.): Boston M. and S. Journ., cxii.

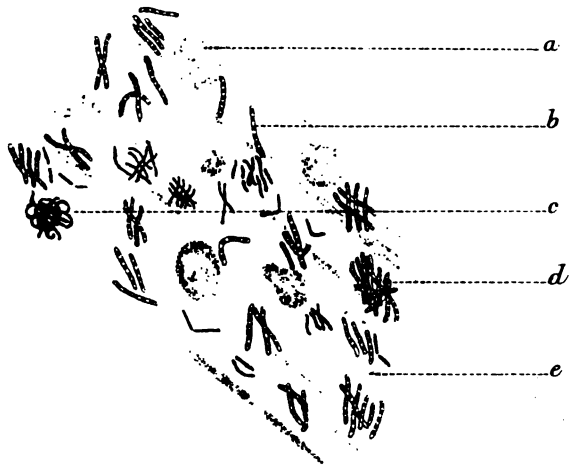


Fig. 86. *Tubercle Bacillus from sputum of girl who died from rapid phthisis. In some parts it seemed to be almost entirely composed of bacillus. a, salivary corpuscle; b, bacillus full of spores, c, rosette-like mass of bacilli not sporing, d, another mass sporing, e, mucus stained with methylene blue. Ehrlich-Weigert process. 1/12 oil immersion, tube out. N° 4 ocular. Hartnack.*

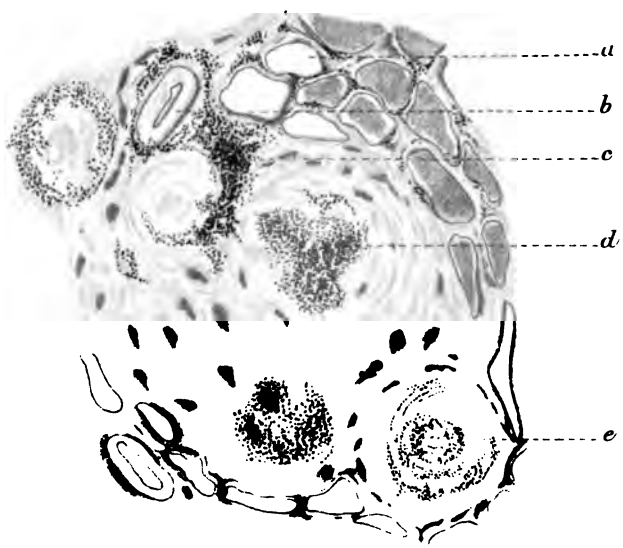


Fig. 87. *Deposit of tubercle bacillus in a phthisical lung. a, air vesicles filled with caseating catarrhal products; b, small artery; c, inhaled pigment; d, the bacillus lying in the centre of a tubercle nodule in process of caseating. Ehrlich-Weigert process without contrast-stain. × 50 Diams.*

1885, p. 265. **Smith** (In Urine): Lancet, 1883, i. p. 942. **Spina:** Wien med. Presse, xxiv. and xxviii. 1883. **Steven:** Glasg. Med. Journ. xix. 1883. **Sticker** (In Blood): Centrabl. f. klin. Med., vi. 1885, p. 441. **Ulacacci** (In Blood): Gazz. d. Osp. Milano, vi. 1885, p. 188. **Vignal:** Bactéries du Tubercle, Gaz. Méd. de Par., iv. 1882. **Weichselbaum** (In Blood): Wien. med. Wochenschr., xxxiv. 1884, p. 333. **Weigert:** Deut. med. Wochenschr., ix. 1883; *also* (Distribution after Inoculation): Jahrb. f. Kinderheil., Leip., xxi. 1884, p. 146. **Whittaker:** Med. News Phila., xli. 1882. **Williams:** Proc. Roy. Soc., xxxvi. 1883-84, p. 510; *also*, Med. Press and Circ., xxx. 1883; *also*, Lancet, 1883, ii. p. 135, *et seq.*

FAVOURITE SEATS OF TUBERCLE.

321. It is a remarkable, and as yet an unexplained, fact, that tubercle has a special affinity for some organs and tissues in preference to, it might almost be said, to the exclusion of, others. Thus certain membranes, such as the **pleura,** the **peritoneum,** the **pia mater,** and the **arachnoid,** are particularly predisposed to its attacks; while others, such as the pericardium, are very rarely the seat of it. The muscular and fibrous tissues enjoy almost complete immunity, and when it occurs in them, as in the case of the pericardium, it is a local disease.[1] Of all organs, the **lung** is admittedly the favourite seat of the disease both in Man and in the lower animals, but the **spleen, kidney, liver, intestine,** and **brain** are very liable to be simultaneously implicated. In the case of the **intestine** the tubercules may be situated either on the serous or on the mucous coat. The mucous membranes of the stomach and of the upper part of the small intestine are peculiarly exempt from its attacks, although, occasionally, a truly tubercular ulcer may be found on the former. **Bone** is frequently tubercular, particularly where a sinus communicates with it. As previously referred to (Sect. 320), it occasionally occurs as a localised deposit within the **blood-vessels** of the lung. Nasse has recorded (No. 13, cv. p. 173, 1886) an infarction-like mass in the kidney and spleen caused by a tuberculosis of the artery leading up to the part; and Vidal (No. 150, Nos. liv. and lv. 1881) refers to what he calls a tuberculosis of the skin, which he says is different from lupus.

Tubercle is remarkable in this respect, that it may constitute a widespread eruption, or may be confined to a particular set of organs or to a special tissue. Thus, in the tuberculosis of children, the disease is usually in the form of an eruption, while in that of adults it more frequently is located in one set of organs, such as the respiratory or the genito-urinary. It is only in comparatively few cases of pulmonary phthisis, in the adult, that the disease sets up a general eruption, even although the lung may be teeming with the bacillus. In the earlier stages of pulmonary phthisis, the lung is, as a rule, the only organ implicated. It is in the later stages of the disease that other organs such as the **larynx** or **intestine** are rendered tubercular, apparently from the bacillus coming into contact with them. The

[1] A case is reported by Annandale (No. 19, 1867) where several cheesy tubercular deposits had formed in the muscles of the arm.

sputum is evidently the vehicle by which it is conveyed in both these cases.

CASEOUS SOURCE OF INFECTION IN ACUTE TUBERCULOSIS.

322. Ever since tuberculosis has been recognised as a distinct disease, it has been noted, in cases where it assumes the character of a general acute eruption, that there is almost invariably a cheesy mass in some part of the body in a state of rapid dissolution. It may be a gland, a cavity in the lung, a peritoneal inflammatory effusion, a caseous testicle, a nodule in the brain, or a strumous abscess. It is manifestly of older date than the tubercle eruption, and it contains the tubercle bacillus. Weber (No. 192, 1869-70) found cheesy foci in sixteen cases of tuberculosis of serous membranes, etc. The absorption of the bacillus from this by the surrounding blood-vessels, is usually regarded as the cause of the acute outbreak of general tuberculosis. The cheesy mass may lie latent so long as it is solid, but as soon as it softens, the poisonous contents can be taken up by the blood-vessels and prove a cause of infection. Hence the danger of all cheesy deposits wherever located.

STRUCTURE OF TUBERCLE.[1]

323. **Naked-eye.**—Although there is a general resemblance in some of the most important macroscopic features of tubercle, yet it by no means follows that they are exactly alike in all organs.

The following may be taken as the *general* naked-eye characteristics :—

(1) The nodules are multiple, either running in lines, arranged in groups, or uniformly scattered through the organ.

(2) They are almost always (in a general eruption) of constant size, namely, that of a millet or mustard-seed.

(3) They are round in shape, and have a sharply-defined border.

(4) They are of almost cartilaginous hardness and lustre.

(5) They can easily be dissected out from the tissue.

(6) Their colour is usually gray, but where the tubercle has caseated it will be found to be more or less cream-yellow.

Microscopic.—As a rule it is a mesoblastic neoplasm, and usually arises from an endothelium such as that of a serous cavity, a blood-vessel, or a lymphatic. A proliferation of this endothelium is the first step in its development, a little mass of highly nucleated cells being thereby produced (comp. Klein, No. 118 ; Buhl, No. 191 ; and Hering, No. 156).

The following are the usual histological forms assumed by the growth—

A. Some very young tubercles are met with in the purely cellular condition just alluded to. They are simple deposits of round cells of

[1] In describing this the author takes as his standard the tubercles which one sees in acute and chronic eruptions.

various sizes, and are mostly to be looked for in very acute eruptions. They are frequently located round a blood-vessel, more especially in the

FIG. 165.—TUBERCLE OF THE LUNG IN A VERY EARLY STAGE OF DEVELOPMENT (×400 DIAMS.)

(*a*) An alveolar wall; (*b*) blood-corpuscles in capillaries of the same; (*c*) blood-corpuscles extravasated into the alveolar cavities; (*d*) alveolar capillaries filled with blood-corpuscles carried forwards by the tubercle, which is growing into the alveolar cavity; (*e*) large endothelium-like cells, of which the tubercle in this stage is mainly composed; (*f*) portion of a branch of the pulmonary artery injected.

pia mater or peritoneum. The tubercle bacillus may be detected in this stage, but with difficulty.

B. Very soon, however, it is noticed that one or more giant-cells appear. These giant-cells are not unlike those of a giant-cell sarcoma, and contain many nuclei. They appear to be, simply, certain of the cells of the mass which have outgrown the others. They sometimes contain the tubercle bacillus in their substance, although rarely in Man, but whether this is the cause of their overgrowth, or whether it is simply that they, being large amœboid bodies, take up any kind of particulate matter in their neighbourhood, is not quite clear. They also absorb pigment particles freely in the same way. The bacillus in such cases is often so small as to resemble a micrococcus. The bacilli are of much more common occurrence in the giant cells of bovine tubercle. There may be several giant cells in a single cellular mass. It generally happens, however, that one has developed more than the others. The most of the tubercles that are encountered in acute eruptions never

FIG. 166.—A GIANT CELL FROM TUBERCLE OF LUNG, WITH INHALED PARTICLES OF CARBON IN ITS INTERIOR (×300 DIAMS.)

(*a*) Central granular part; (*b*) peripheral pigmented portion.

proceed further in development than this stage. There is a great liability for the cellular mass to *caseate* when it has proceeded so far, and this effectually puts a stop to its complete evolution. Lying within the caseous part may sometimes be seen the tubercle bacillus. It usually increases in quantity, and in the frequency with which it occurs in individual tubercles, as caseation progresses. There are many nodules, however, as before mentioned, in which not a vestige of the bacillus is to be seen.

The little mass appears to be quite devoid of blood-vessels, and it is a question as to whether this or the presence of the tubercle bacillus is the cause of the caseous necrosis.

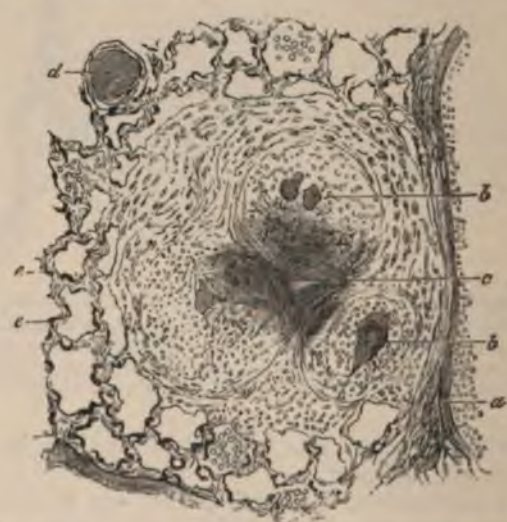


FIG. 167.—PRIMARY TUBERCLE OF LUNG, TWO TO THREE WEEKS OLD (×50 DIAMS.)

Source of infection was a caseous peritonitis. (*a*) Portion of wall of a branch of the pulmonary artery; (*b*, *b*) giant cells with concentric arrangement of fibrous tissue; (*c*) centre of tubercle beginning to caseate; (*d*) small branch of pulmonary artery seen on transverse section; (*e*) injected capillaries of the alveolar walls.

C. Sometimes, more particularly in chronic tuberculosis of the lung, the tubercle does not caseate, but continues to live on and develop into what seems to be its ultimate stage of organisation. In the centre, or nearly so, is usually a large giant cell, while around this there may be several smaller ones. From the periphery of the giant-cell processes come off, which after radiating from it for a certain distance, begin to divide and subdivide. This subdivision of the processes in course of time produces a reticulum whose meshes vary in size. Towards the margin of the tubercle the reticulum becomes condensed, and forms what might be termed a *capsule* for the tumour. It is this capsule which gives to old tubercles their sharp boundary margin. Within

the meshes of the reticulum lie two kinds of cell. The one is small and round, and goes generally by the somewhat ambiguous designation of a *lymphoid corpuscle*. The other is larger, and is usually termed a *small giant cell*. The giant cells are finely granular, and show large numbers of minute oval-shaped nuclei either aggregated in a mass at their centre, or arranged in a crescent at one end. Wagner (No. 123) was the first to describe this peculiar reticular giant-cell system.

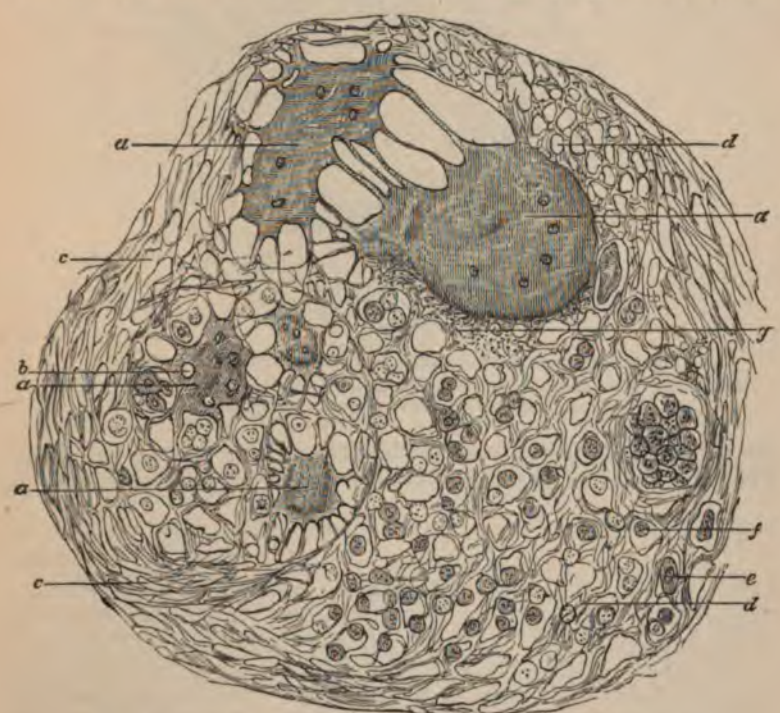


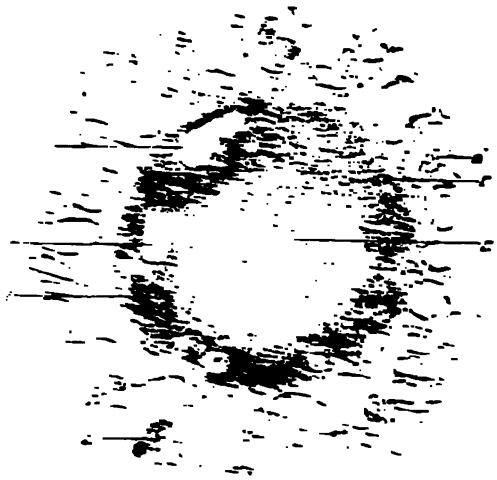
FIG. 168.—FULLY DEVELOPED RETICULAR TUBERCLE OF LUNG (×450 DIAMS.)

(*a*, *a*, *a*) giant cells; (*b*) vacuole in one of these; (*c*) peripheral capsule of fibrous tissue; (*d*) reticulum of the tubercle; (*e*) large endothelium-like cells lying on the reticulum and within its meshes; (*f*) smaller "lymphoid" cells occupying the same situations; (*g*) peripheral fibrous-looking border of the giant cell.

Schüppel (No. 152), in the same year, also drew attention to the reticular arrangement within tubercles of lymphatic glands. Gaule and Tizzoni (No. 13, vol. lxiii. p. 386) distinguish three zones in a tubercle: (1) an external, composed of small round cells; (2) a lesser, epithelial, or middle zone containing the reticulum; and (3) a central space containing a giant cell.

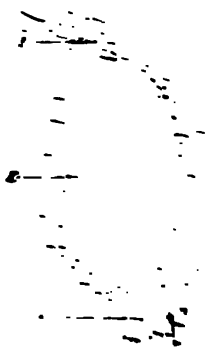
D. If the tubercle is still older, this reticular giant-cell system, as it is called, disappears, and is replaced by a simple mass of fibrous

[illegible] The manner in which this metamorphosis is accomplished is the following. The giant cell becomes more and more fibrous towards



[illegible]

the [illegible] of the [illegible] part in the centre. The [illegible] becomes transformed into or



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[illegible] the fibrous margin. This [illegible] is covered with [illegible] which appear to be [illegible] from the giant cell. In course

of time, the previously uniform fibrous border splits up into bundles, the nuclei still lying upon them. The fibrous transformation ultimately seizes upon the protoplasmic remains of the giant cell in the centre, so that the whole giant cell and tubercle nodule become converted into a mass of fibrous tissue. This cicatrisation, if it may be so called, in fact represents the healing of the tubercle, and is the natural course it follows if its full development is not interrupted by

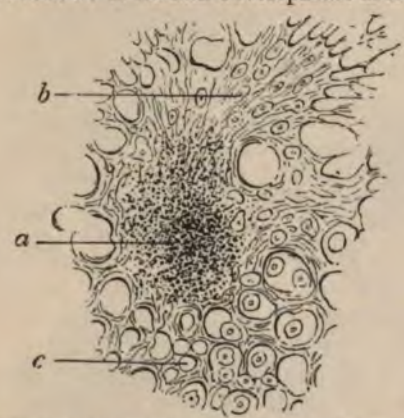

FIG. 171.—REMAINS OF A GIANT CELL IN PROCESS OF FIBROUS TRANSFORMATION (×400 DIAMS.)

(*a*) Some of the central protoplasmic part still remaining; (*b*) the peripheral portion, which has now become developed into reticular fibrous tissue, nuclei are seen lying upon it; (*c*) the reticulum constituted by the fibrous periphery.

caseation or other contingency. In this stage, the tubercle bacillus vanishes.

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DEGENERATIONS.

324. (1) *Caseous.* This is by far the commonest, and it invariably commences at the centre of the growth. The cause of its frequency is explained on a double basis; firstly, that tubercle is a non-vascular

growth, and secondly, that the tubercle bacillus contained within it tends to deprive the tissue of nourishment, and hence favours necrosis. Probably both factors have to do with it.

(2) *Fibrous.* The conversion into fibrous tissue can hardly be re-

FIG. 172.—OLD FIBROUS AND RETICULAR TUBERCLES OF THE LUNG (×50 DIAMS.)

(*a*, *a*, *a*, *a*) Four tubercles; (*b*) thickened interstitial tissue uniting two tubercles; (*c*) giant cells; (*d*) giant-cell reticulum; (*e*) centre of a tubercle caseating; (*f*) a giant-cell system which has become converted into a mass of hyaline fibrous tissue.

garded as a degeneration, seeing that it is the natural termination of all truly tubercular nodules.

(3) *Hyaline.* After being converted into fibrous tissue, the nodules sometimes become unnaturally transparent, evidently from hyaline degeneration (Sect. 136, see also Fig. 172, *f*).

GLANDULAR COMPLICATION.

325. The glands connected with tubercular organs usually become enlarged, and the enlargement is almost always due to tubercular contamination. When they are incised, little gray points are found scattered throughout their substance. At other times, where the tubercles are very abundant, they have a shining, homogeneous appearance, almost as if they were waxy; on microscopic examination it will be found that the cause of this is a diffuse tubercular infiltration. The giant cells in these tubercles of lymphatic glands are often very beautiful.

Preparation.—This depends a good deal on what it is desired to bring out. To demonstrate the bacillus, harden in "A," and stain by the Ehrlich-Weigert, Ziehl-Neelsen, or other method (see Sect. 84); clarify in oil of cloves, followed by oil of bergamot or xylol, and mount in Canada balsam or gum dammar dissolved in xylol. The colour of the bacillus is much more permanent in xylol balsam or dammar than in lac prepared with chloroform and turpentine, or when an excess of oil of cloves is left in the preparation. It will be found, however, that the individual bacilli are not so evident with high powers, when mounted in this medium, as when examined simply in oil of cloves, the loss in definition being due to diminished transparency. To see the characters of the caseous centre, harden in "C," followed by "A"; stain in perosmic acid, and mount in Farrants' solution. This method does also excellently for the demonstration of the reticulum. The general characters of the tumour, as seen with a low power (50 diams.), may be beautifully demonstrated by hardening in "A"; staining in hæmatoxylene, followed by eosin spirit; clarifying in oil of cloves; and mounting in solution of gum dammar.

Preparation of Sputum (see Sect. 88).

ARTIFICIAL TUBERCULOSIS.

326. If an animal, such as a guinea-pig or rabbit, be inoculated subcutaneously with the contents of a softening cheesy deposit containing the tubercle bacillus, it develops a tubercular eruption in most of its organs within a fortnight to six or eight weeks.

Method.—A small incision should be made into the skin of the neck or back; the cellular tissue is to be separated for some distance so as to form a sinus-like pouch; and into this some of the infecting material should be introduced on an öse (Sect. 75). Either the contents of a cheesy cavity, tubercular sputum, or a cultivation of the bacillus may be employed. They may also be injected subcutaneously if a mixture in water, or in $\frac{3}{4}$ per cent salt solution, is used as a vehicle.

A cheesy abscess-like cavity will usually be found at the point of inoculation after from three weeks to a month, and the neighbouring

lymphatic glands will be seen to be swollen and to contain tubercles. Within the lung there is generally an abundant eruption of minute gelatinous or cheesy nodules.

Lung.—According to Klein (No. 118), artificial tuberculosis in the lung of the guinea-pig is characterised by the formation of bands of adenoid tissue around the alveoli, and, subsequently, by the production of nodules having an intra-alveolar site. The first change, probably, consists in a proliferation of the endothelium of a branch of the pulmonary artery, thus forming a small nodule. The neighbouring lymphatics subsequently become filled with adenoid cells, giving rise to the appearance of lymphadenoid cords. The epithelium within the alveoli also proliferates so as to cause nodular deposits; these afterwards caseate, but the cord-like lymphadenoid deposits never do.

Peritoneum.—When the inoculation is made into the peritoneal cavity, it occasions a more or less diffuse peritonitis, with a tubercle eruption over the peritoneum. It may ultimately end in a general tuberculosis. Klein (*loc. cit.*) describes the nodules as growing from the endothelium of the surface, with a stoma in their centre. The lymphatic vessels later on become highly tubercular.

Eyeball.—When injected into the anterior chamber of the eye, a tubercularisation of the iris follows, with, it may be, in course of time, a general tubercular eruption.

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LIABILITY OF DIFFERENT ANIMALS.

327. Of all animals the rabbit[1] and guinea-pig seem to take the disease most readily. Horned cattle die from the disease in large numbers, especially those technically described as "deep milkers," but the dog and cat are less susceptible to it. The horse, mule, and ass do not seem to become frequently tubercular, but all the quadrumana

[1] It has been suggested by Waldenburg (No. 168, p. 167) that as rabbits drink little if any water they are more liable to a dry cheesy metamorphosis than other animals. It is a curious fact that excessive beer drinkers seldom die from caseous phthisis.

are very liable to its ravages, and are readily inoculable (Krishaber and Dieulafoy, No. 153, No. 34, 1881).

The disease in cattle is known in Germany as "Perlsucht" or "Franzosen-Krankheit," and in this country it goes by various unscientific names, but usually, at the present day, simply by that of "tuberculosis." As in Man, it is sometimes localised to a particular set of organs, such as the digestive; or it may be general, in which case, the serous membranes largely participate. Veterinary surgeons affirm that it is more common in highly bred animals than in those of coarser grain, and that there are certain characteristics by which they can prognose, as in the human subject, what animals will be likely to fall victims to it. For long it was doubtful whether "Perlsucht" and human tuberculosis were alike and due to the same poison. Schüppel (No. 13, lvi. p. 38) and others, however, showed that the nodules in both have an identical structure, and, since then, the tubercle bacillus has been found abundantly in the former. Lydtin (No. 49, i. 1884, p. 591), from his researches, has made out a complete identity in the two diseases in regard to their contagiosity, structural peculiarities, and geographical distribution. Virchow (No. 43, 1880, Nos. xiv. and xv.), however, has drawn attention to the fact that the "Perlsucht" nodules become very hard and fibrous, have little tendency to caseate, but readily calcify. In human tuberculosis, on the other hand, caseation is the rule, and calcification is uncommon.

CONTAGIOSITY OF TUBERCULOSIS.

328. Villemin (*loc. cit.*) was the first to clearly demonstrate that cheesy tubercular deposits are inoculable. Since then the numerous experiments that have been made clearly point to its being one of the most contagious of diseases. Toussaint (No. 40, T. 93, No. v. p. 281) from his many experiments on various animals, concludes that no disease is more readily inoculable than tuberculosis, and that the susceptibility of rabbits to it is as great as in the case of anthrax. All the **liquid secreta** of the bodies of tubercular animals are bearers of the poison, and a transference of these to sound animals induces tuberculosis. The poison, moreover, can be maintained at a temperature which destroys the anthrax bacillus. He thinks (No. 40, T. 93, No. vi. p. 322) that cattle kept in stalls close together become rapidly tubercular from contagion.

MEANS OF CONTAMINATION.

329. The channels by which the tubercle poison may gain entrance to the body are numerous. The chief of them are the following:—

A. **By Inoculation.**—When the poison is introduced subcutaneously, the disease is reproduced with great certainty (see Sect. 326). It is remarkable, however, that the contraction of the disease through super-

ficial wounds of the skin in the human subject is rare.[1] Pathologists working often for hours at a time with their hands immersed in the contents of phthisical cavities, have never been known to become generally tubercular from this cause.[2] It has been asserted that the tubercle bacillus is present in certain dissection wounds, but further confirmation of this would seem to be required. If it be present, for some unknown reason, it does not tend to spread into the system generally, but remains localised to the point of inoculation. It would be extremely interesting to know whether those dissection wounds having a peculiarly indurated character, and which are very intractable, are tubercular.

B. **Through the Ingesta.**—There cannot be the slightest doubt that contaminated food may be a fertile source of communicating the disease. Orth (No. 13, lxxvi. p. 217) showed that if rabbits have "Perlsucht" tissues mixed with their food they rapidly become tubercular, the tubercles showing themselves on the pharynx, intestine, lung, and serous membranes. Semmer (No. 159, 1877) experimenting on something like one hundred dogs with the tissues of thirty tubercular cows, was unsuccessful in inducing it. He concluded that the dog enjoyed an immunity to the attacks of the disease through this channel. Lange (No. 160, 1880, p. 309) was more successful with rabbits, dogs, and fowls, using the tubercular tissues of animals dead from Perlsucht. Klein and Gibbes (No. 161, 1884–85) found that although guinea-pigs are affected both by bovine and by human tubercular matter, they are more susceptible to the latter than to the former. With rabbits, on the other hand, the susceptibility is reversed. Fischer (No. 104, xx. p. 446, 1886) showed that the tissues of tubercular rabbits are highly contagious when a solution of them is swallowed by other rabbits.

Phthisical sputum is eminently contagious when swallowed. As Klebs and Valentin pointed out, it is through swallowing the expectoration that the intestinal mucous membrane becomes tubercular in pulmonary phthisis. Wesener (No. 158) rendered a large proportion of rabbits tubercular by feeding them on phthisical sputum. Klein and Gibbes (*loc. cit.*) were similarly successful. Dried sputum, according to Wesener, is equally virulent. The bacilli in all cases were found abundantly in the nodules.

Instances of direct contamination from the sputum of a *phthisical mother* or *nurse* have of late been recorded. Herterich (No. 162, No. xxvi. 1883) describes the case of a widow, formerly healthy, who was married to a phthisical man. Two children born of the first marriage as well as the first of the second marriage remained free from any disease. The two following children were sound during the first months of their life. Symptoms of phthisis afterwards showed them-

[1] Bollinger, Koch, and Schmidt have specially drawn attention to the difficulty of inoculating tubercle merely through scratches of the skin.

[2] See suspected case by Verneuil, No. 153, xiii. 1884.

selves in the mother, and, upon this, both of the last mentioned children became tubercular. At the autopsy on the children, cheesy bronchial glands were found, along with numerous cheesy nodules in the lungs, spleen, liver, and kidneys. The children had been nourished at the breast, and, later on, with food which the mother had previously chewed. The commencement of the disease in the children was traced to the presence of deep yellow coloured ulcers on the mouth and throat.

Another remarkable case is recorded by Reich (No. 43, No. xxxvii. 1878). In Neuenburg, a village of 1300 inhabitants, the midwifery practice was divided between two women, one of whom was phthisical, and ultimately died from the disease. Of the children delivered by this woman, from 11th July 1875 to 29th September 1876, no less than ten died of tubercular meningitis, and not a single one with a hereditary history. In the practice of the other midwife no such mishap came to pass. Both were in the habit of removing mucus in the air-passages from the newly-born child by aspiration, and they established respiration by blowing air into the mouth.

De Lamallerée (No. 49, ii. Ab. i. p. 124) relates the following instance of supposed infection. A soldier returning home imported the disease into an isolated spot, where previously it was unknown, and infected his wife with it. Later on, a robust woman, having little immediate communication with them, became infected. It was found that she had received fowls from the man and his wife which had been allowed to consume the sputa, and that one of the fowls, examined by De Lamallerée, proved to be tubercular. As many as sixteen of these fowls had been consumed in a half-cooked state during four months.

Milk from tubercular cows seems to be a certain means of inducing tuberculosis when ingested. It is most virulent when taken from a cow suffering from tubercular disease of the udder, but even when derived from a tubercular animal in which the udder is sound, it is capable of exciting tuberculosis in animals fed on it. According to Bang (No. 160, 1885, p. 45) and Bollinger (No. 163, No. xvi. 1883, and No. 49, i. 1883, p. 626), the bacilli are abundant in the milk from such udders.[1] They mostly contain spores. For a month or so after the disease has commenced, the milk continues to be apparently unaltered, even although it may prove to be highly contagious. It subsequently becomes thin and serous.

Peuch and Toussaint (No. 154, No. xv. 1880) rendered pigs tubercular within thirty-five days by feeding them on milk taken from a tubercular cow. Bang (*loc. cit.*), Bollinger (*loc. cit.*), and Wesener (*loc. cit.*), have had similar experience. The tuberculosis is chiefly located in the *intestinal mucous membrane* and in the *mesenteric glands*. It is a question to be solved in the future, as to whether the tabes mesenterica of children may not be due to a similar cause.

Tubercular Udder.—Bang (*loc. cit.*) states that the tubercular udder

[1] The author has confirmed this observation.

in cows is not so rare as might be supposed. A diffuse painless tumour forms in one or other quarter of the gland. The large size of the udder, its unusual hardness, and the complete absence of signs of suppuration are distinctive diagnostic features. At first, the disease appears to be a diffuse infiltration, but soon, distinct yellow cheesy nodules show themselves in it. Within the large milk ducts are numerous nodules which contain the bacillus abundantly. The latter is discharged in quantity into the secretion. In from two to four months the animals die in an emaciated condition.

Tuberculosis of Human Mamma.—Cases of this disease in the human female have been recorded of late by Dubar (No. 165) and Durel (No. 166, No. ix. 1882), and by Poirier (No. 167) both in the female and male. In nearly all the cases the disease begins as an **abscess** which opens and leaves a sinus which will not heal. Cheesy masses are found in the gland, and the neighbouring lymphatics of the axilla and root of the neck become swollen and caseate.

Cooking of the flesh of tubercular animals must be very thorough in order to destroy its virulence. Toussaint (*loc. cit.*) found that when pieces of the muscle of a tubercular sow were cooked over a gas flame like a beef-steak, the juice squeezed out of the flesh was capable of infecting rabbits, when administered to them.

Locality.—In all feeding experiments, the stomach and upper part of the intestine enjoy a remarkable immunity from the attacks of the disease, while the lower part of the small intestine suffers most. Wesener (*loc. cit.*) states that the spores when swallowed are capable of withstanding the action of the gastric juice, while the bacilli are destroyed by it.

C. **By Inhalation.**—When liquids containing the tubercle bacillus are sprayed into a confined chamber, and animals of various kinds are allowed to breathe the atmosphere, they rapidly become tubercular.

Schottelius (No. 13, lxxiii. p. 524), Tappeiner (No. 13, lxxiv. p. 393), Wargunin (No. 13, xcvi. p. 366), and Weichselbaum (No. 50, No. xix. 1882), have shown that animals made to breathe phthisical sputum rarefied throughout an atmosphere by means of a spray-producing apparatus, even after only a few inhalations, readily become tubercular. The time intervening between the inhalation and the advent of the tuberculosis, is almost the same as that required for the production of the disease by inoculation. The lung suffers most, but other organs also participate. The nodules in the lung have the character of little lobular intra-alveolar deposits. Sputum not containing the bacillus gives negative results.

Tubercle bacilli have been found in the *atmosphere* of apartments in which phthisical patients were living.

Schmidt (No. 162, Nos. xlvii. and xlviii. 1883), collecting the dust of such apartments by allowing it to fall upon plates of glass coated with glycerine, was unable to reproduce tuberculosis in rabbits by inoculation.

D. Tuberculosis from causes other than the Tubercle Poison.—When substances other than tubercular products are inhaled by, or are inoculated upon, rabbits and guinea-pigs, they frequently occasion a tubercular or tubercle-like eruption. *Pieces of sponge* placed in the abdomen readily excite it, and it has been asserted that *powdered glass* has a similar property. Schottelius (*loc. cit.*), Wargunin (*loc. cit.*), Weichselbaum (*loc. cit.*), and Martin (No. 4, No. i. p. 49, 1882), have employed various substances by way of experiment—such as *powdered cheese*, *brain substance*, *lycopodium seed*, *cayenne pepper*, and *pulverised cantharides*. They caused these to be inhaled in the form of a fine spray, with the result that they were almost invariably able to produce in different animals an eruption of tubercle-like nodules in the lung and sometimes in other organs. Those in the lung seemed to be, in most cases, of the nature of little catarrhal pneumonic masses, with, in some instances (Schottelius), peribronchial lymphoid cords or nodules. With *Limburger cheese* Weichselbaum occasioned an eruption in the lungs and kidneys of dogs after fifteen inhalations during seventeen days, indistinguishable from that resulting from the inhalation of tubercular materials. *Boiled tubercular sputum*, when introduced into the abdomen, usually failed to induce tuberculosis.

There is, therefore, no doubt that various organic substances introduced into the tissues or inhaled, can induce in rabbits, guinea-pigs, and other animals, a disease very much like tuberculosis. Koch, however, asserts that this cannot be transmitted, and, therefore, must be something different from true tubercle.

Cheyne (No. 193, April 1883) explains many of these cases on the supposition that the substances employed are contaminated with the tubercle bacillus before being introduced, and asserts that, when they are sterilised, tuberculosis does not follow.

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TUBERCLE AND SCROFULA.

330. It was long supposed that scrofulous deposits were something different from tubercular. Of late years, however, the recognition of the fact that tuberculosis may be localised to a particular tissue or organ has tended to do away with this distinction. Baumgarten's inoculation experiments (No. 93, No. xxii. 1882) seem to show that the whole three diseases, Perlsucht, Tubercle, and Scrofula, are alike, in so far at least as they contain a common virus. Grancher (No. 150, Nos. liv. and lv. 1881) is of a like opinion.

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PSEUDO-TUBERCULOSIS.

331. Under this name, Eberth (No. 13, c. p. 15, 1885; *also Ibid*, ciii. p. 488, 1886) has described a peculiar disease of guinea-pigs and rabbits, which in its general features resembles tuberculosis, but differs from it, in that the tubercle bacillus is absent.

The abdominal organs are most affected, and many of the lymph glands are enlarged and caseous. The disease manifests itself as a nodular eruption, each nodule being very minute. The nodules are either isolated or in groups, and are situated in the various abdominal organs. The liver appears to be the head-centre of the disease. It is usually cirrhosed, and in the midst of the cirrhotic tissue are cheesy foci, while in the immediate vicinity of these are little cellular nodules similar to those seen in other parts. The disease of the liver is evidently older than that of other parts. It is not due to an animal parasite such as a cysticercus or pentastoma, nor do the nodules contain psorospermia.

It differs from tuberculosis in the fact that there is little tendency to the disease spreading into the lung; the bronchial glands are not usually affected; and, if so, only in a minor degree. In spontaneous tuberculosis of these animals the lung is, as a rule, the chief focus of the deposits.

The nodules appear to contain several organisms, or, at any rate, several stages in the development of a bacillus differing from that of tubercle both morphologically and in its reaction with staining reagents.

A similar disease was set up in the guinea-pig by Malassez and Vignal (No. 4, 1883 and 1884) through the subcutaneous inoculation of tubercle taken from a tubercular meningitis in a child. It was easily reinoculable, and contained no tubercle bacilli, but zooglœa masses of a bacillus were in abundance. They named it "tuberculose zoogléique."

Preparation.—The organisms are with difficulty coloured by ordinary methods. Eberth recommends Löffler's stain as the best; it colours them brilliantly. Stain in a mixture of 100 c.c. potash solution (1 : 1000) and 30 c.c. saturated solution of methylene blue for from six to seventy-two hours. Wash out with acidulated water (5 drops glacial acetic acid to 20 c.c. distilled water) for from one to two minutes; and, subsequently, with alcohol (80 per cent) for a like time. Clarify by the usual means.

LUPUS.

332. This is a skin disease about the pathology of which there was, until lately, considerable difference of opinion. There does not seem to be much doubt now, however, that the disease is closely allied to tubercle, if not identical with it—a localised tuberculosis.

Sites.—These are chiefly upon the nose and cheeks, but it may also grow upon the skin of the buttocks, extremities, or trunk.

General Characters.—It commences in the form of several small red vascular nodules which are not painful. They increase in size and extent, and become covered with white epidermic débris. If the lupus is of the variety known as "non-exedens," these nodules in time simply cicatrise, and leave a firmly contracted scar often causing much deformity. The nodule, however, more commonly ulcerates and erodes the tissue (lupus exedens). The ulcer continues to spread in one part and to cicatrise in another.

Nature of the Disease.—Various conjectures as to its nature were

FIG. 173.—SECTION THROUGH A LUPUS NODULE OF THE NOSE.

formerly made by Virchow, Auspitz, and others, but it was not till Friedländer (No. 13, 1874) published his paper on the subject, that it was suspected to be tubercular. He found that the nodules contained a giant-cell structure similar to that of tubercle (Sect. 323, C). Thin (No. 34, lxii. 1879) and others have confirmed these observations.

Not only have the nodules sometimes the reticular character of a tubercle, but Koch (No. 44, vol. ii.) has demonstrated the tubercle bacillus in them. It is very sparsely distributed, however; so much so, that he met with it in only one out of twenty-seven of a particular set of preparations, and in only one out of forty-three preparations in another. He was, however, able to make a pure culture of the bacillus from it. Vidal (No. 150, Nos. liv. and lv. 1881) describes a disease which he calls "tubercle of the skin." It corresponds histologically with lupus, but differs from it in being readily inoculable.

The neighbouring lymph glands become implicated, and Friedländer has shown that their enlargement is not due merely to a lymphadenitis but to multiple small tubercle nodules.

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SYPHILITIC GUMMATA.

333. **Definition.**—*A gumma is a portion of a tertiary syphilitic inflammatory deposit which has undergone caseation in a peculiarly circumscribed manner.*

It should not, strictly speaking, be classified among the neoplasms, seeing that, in reality, it is merely a *degeneration* of a tissue resulting from a peculiar form of inflammation.

General Description.—They are cream yellow masses of doughy or almost horny consistence, with a sharply defined border. They do not occur in an otherwise sound part, but are an accompaniment of the peculiar cirrhosis, to which the lung, liver, and other organs and textures are subject in tertiary syphilis. The gummata are pieces of the newly formed granulation or young cicatricial tissue, which have necrosed and caseated. The dense semi-fibrous basis in which they lie is usually arranged concentrically around them, so as to construct a spurious capsule from which they can sometimes be enucleated. They vary in size from a millet seed to that of a walnut, and are, sometimes, quite round; while, at other times, they present a sinuous outline.

Microscopically, the caseous centre is amorphous, and will be found to be without any vestige of cells or fibres, provided that the caseation is complete. When the gumma is incipient, the fibres of the newly deposited cicatricial tissue become at first dusky and granular, but are still seen to be continuous with the parts in the neighbourhood. At a later period, a complete separation of the living from the dead ensues. The enveloping tissue is usually like that found in any young cicatrix, with this exception, that its small round cells are aggregated in heaps or dépôts in certain localities, particularly in the immediate vicinity of the caseous part.

The ARTERIES found in the closely adjacent sclerosed tissue usually show great thickening of their tunica intima, so considerable as, in many instances, to amount to complete obliteration of their lumen. This has been alleged to be the cause of the necrosis, and, doubtless, the peculiarly sinuous border which gummata frequently exhibit, has a certain resemblance to that of the territory of distribution of a small artery.

Sites.—The liver, kidney, spleen, periosteum of long bones such as the tibia, and that of the flat bones of the skull, are the favourite

localities. Certain cirrhosed lungs, in which gummatous-looking cheesy masses are present, appear to be syphilitic in their nature. (See Greenfield, No. 192, 1876.)

Absorption.—Gummata are in course of time removed, but not by softening. The necrosed tissue is gradually absorbed from the border inwards, a little calcareous mass being often all that is left to mark its site.

Bacillus.—Lustgarten (No. 45, Nov. 12, 1884; No. 46, i. 1885;

FIG. 174.—GUMMATOUS HEPATITIS (×40 DIAMS.)

(*a*) Caseous centre of the gumma; (*b*) small-cell infiltration round about it; (*e*, *e*, *e*) obliterated arteries; (*d*) small artery with hypertrophied middle coat (Hæmatoxylene and Eosin).

and No. 47, March 27, 1885) has demonstrated the presence of a bacillus in chancres and in gummata, resembling that of tubercle, which he regards as being specific. This has also been held by some to be the cause of the caseous necrosis. (For further particulars see "Hard Chancre," and Practical Bacteriology, under "Staining").

Preparation.—Harden in "A." Stain in hæmatoxylene, and mount in Farrants' solution; or harden in "A," and stain in perosmic acid and picro-carmine. Mount as before. To stain the bacillus consult Sect. 85, Part I.

Literature on Syphilitic Gumma.—Consult text-books enumerated at p. 345 and p.— **Cornil**: Syphilis (transl.), 1882. **Bäumler**: Cycl. Pract. Med., v. Ziemssen, iii. 1875, p. 2. **Hamilton**: Lectures on Syph. Osteitis and Periostitis, 1874. **Heubner**: Die luetische Erkrankung d. Gehirnarterien, 1874. **Lancereaux**: Treatise on Syphilis

(transl.), N. Syd. Soc., 1868-9; *also*, Gaz. d. hôp., 1876. **Lang**: Wien. Med. Presse, xxv. 1884, pp. 1176, *et seq.*; *Ibid.*, xxvi. 1885, pp. 9 and 43. **Greenfield** (Several Memoirs on Arteries, Gummata, Syph. Pneumonia, etc.): Trans. Path. Soc. Lond., 1876-77. **Oppert**: Visceral and Hered. Syph., 1868. **Virchow**: Arch. f. path. Anat., xv. 1858, p. 217; *also*, Die krankhaften Geschwülste, ii. p. 393. **Wagner**: Arch. d. Heilk., iv. 1863, p. 1, *et seq.*; *Ibid.*, v. p. 121. **Wilks**: Trans. Path. Soc. 1858, *et seq.*

Literature on Syphilitic Bacillus.—**Alvarez and Tavel**: Progrès Méd., ii. 1885, p. 135; Arch. de Physiol., vi. 1885, p. 303. **Cornil**: Bull. Acad. de Méd., xiv. 1885, p. 1039. **Doutrelepont and Schütz**: Deut. med. Wochnschr., xi. 1885, p. 320; Centralbl. f. Chirurg., xiii. 1886, p. 65. **Giletti**: Gior. ital. d. mal. ven., xxvi. 1885, p. 282. **Hugo-Marcus**: Nouvelles Recherches sur le Microbe de la Syphilis, 1885. **Klemperer**: Deut. med. Wochnschr., xi. 1885, p. 809. **Lustgarten**: Wien. med. Wochnschr., xxxiv. 1884, p. 1389; *Ibid.*, xxxv. 1885, p. 517; Lancet, 1885, i. p. 609; Die Syphilis-bacillen, 1885. **Zeisler**: Chicago Med. Journ. and Exam., i. 1885, p. 113. **Zeissel**: Wien. Med. Presse, xxvi. 1885, p. 1512.

General Instructions for Examining Tumours.

334. The greatest care must be exercised in pronouncing upon the nature of any tumour. The life of a patient frequently hangs upon the opinion arrived at, and hence an error in diagnosis and prognosis by the operating surgeon is much to be deplored, and, in most instances, is inexcusable. The mamma may be cited as an organ in which a correct estimate of the course a tumour located in it will probably take, comes to be of extreme importance, and as being a field in which mistakes in this very direction are so common. The following suggestions may serve as an aid in the examination of tumours generally; detailed instructions for the examination of tumours of special organs, such as the mamma, will be found along with the description of the diseases of the organ concerned.

1. **Recent Examination.**—If there is any doubt as to the nature of a neoplasm, it may be well to excise a small portion before its complete removal. If this is not deemed advisable, and if the tumour has been excised *locally* on the strength of its presumed benignity, make a small section of it in the ether freezer, and examine it before closing the wound.

2. **Clinical History.**—Always inquire into this before coming to a conclusive opinion. The rapidity of growth, whether it has recurred after a previous removal, etc., are points of the greatest moment.

3. **Locality.**—Take notice whether it has arisen from the *epithelium* covering an exposed surface, or from a *gland* lined by epithelium; or whether it has sprung from a tissue of mesoblastic origin, such as a bone, fibrous tissue, muscle, etc. Remember the difference between an epithelium and an endothelium (Sect. 305).

4. **Naked-eye Appearance.**—Be extremely careful in pronouncing upon the nature of a new growth from *microscopic examination* alone. Carefully note whether it has a border sufficiently sharp to allow of its being enucleated. If so, the probabilities are that it is not a *primary cancerous tumour*, but that it belongs to the *connective tissue class*. *Secondary* cancerous tumours sometimes have a sharp border, *primary*

seldom if ever. Then notice its consistence, colour, surface markings, the presence or absence of fat tissue in its midst, the occurrence of hæmorrhages. Cancers are seldom hæmorrhagic; the sarcomata frequently are. The presence of true melanine is also of course a strong indication of its belonging to the connective tissue class.

5. **Microscopic Examination of Hardened Tumour.**—Most of the tumours are best hardened in spirit (see Special Tumours). Cut the sections in the freezing microtome, stain with various reagents, mount some of them in Farrants' solution, clarify others and mount in solution of gum dammar. Always examine the tumour with a low power (45 to 50 diams.) before proceeding to the further examination with one higher (300 to 450 diams.) In the general scan of the preparation obtainable with the lower power, notice whether it is chiefly cellular, fibrous, or a mixture of the two. If cellular, observe the general shape and size of the cells so far as this can be done with the magnifying power employed. If fibrous, try to make out whether the fibres are composed of white fibrous tissue, muscle, etc. If a mixture of the two, note (*a*) whether the fibres form meshes which contain the cells, and, if so, whether the cells spring from the walls of the fibrous alveoli (*e.g.* alveolar sarcoma), or whether they merely pierce into the fibrous interspaces (*e.g.* cancer). Also, whether the cells tend to form fibres, and whether the fibrillation is going on more actively at certain parts of the tumour than at others. With the high power, complete the examination on the same lines. Take special note of the presence or absence of the histological *signs of malignancy* previously mentioned (Sect. 274).

335. Table of Classified Tumours.

Benign	A. *Simple Histioid.*		
		Fibroma	Mesoblastic, and of fibrous tissue type.
		Molluscum fibrosum	
		Neuroma (fibrous)	
		Painful subcutaneous tubercle	
		Lipoma—type in adipose tissue	Mesoblastic.
		Chondroma—type in cartilage	
		Fibro-chondroma—type in white fibro-cartilage	
		Osteoma—type in bone	
		Myoma—type in muscle (striated and unstriated)	
	B. *Compound Histioid Tumours.*		
		Blood-angeioma—type in a blood-vessel	Mesoblastic.
		Aneurism	
		Lymph angeioma—type in a lymphatic vessel	
		Neuroma (true)—type in a nerve-ganglion	Epiblastic.

C. *Sarcomata.*

Malignant . . .	Round-cell Giant-cell or Myeloid Glioma Alveolar Sarcoma Angeio-Sarcoma Malignant Epulis Melanotic Sarcoma Cylindroma Lympho-sarcoma Psammoma (?)	Mesoblastic.

D. *Epitheliomata.*

Usually benign but may become malignant .	Papilloma Adenoma	Epiblastic, Hypoblastic, and Mesoblastic (?)
Benign . .	Cutaneous horns	
Malignant . . .	Cancer	

E. *Tumours due to action of a Vegetable Micro-organism.*

Tubercle	Gumma (?)
Lupus	Condyloma (?)

F. *Anomalous Tumours of various Construction.*

Malignant and Benign	Cysts Polypi

General Literature on Tumours.—**Abraham** (Blood-vessels of New Growths): Trans. Acad. Med. Ireland, 1883, i. p. 145. **Bard** (General Path. Anat.): Arch. de Physiol. norm. et path., v. 1885, p. 247. **v. Bergmann** (Congenital Sacral Tumours): Berl. klin. Wochnschr., xxi. 1884, pp. 761, 780. **Beyer:** Beiträge, z. Casuistik d. congen. Sacraltumoren, 1885. **Billroth:** Surgical Pathology, N. Syd. Soc., 1877-8. **Bollinger** (Tumour-forming Fungus in Horse; *micrococcus botryogenus; betryomycosis*): Sitzungsb. d. Gesellsch. f. Morphol. u. Physiol. in München, 1887, iii. p. 5. **Butlin** (On Malignant Disease; Tumours): Holmes' Surg., 1883; *also*, Ashurst's Encycl., iv. 1884. **Filbry:** Ueb. indirekte Zelltheilung in path. Neubildungen, 1886. **Glogner:** Ueb. congenit. Sakraltumoren, 1883. **Guillabert:** Étude critique des classifications d. tumeurs, 1885. **Hall** (Contributions to Etiology of Malignant T.): Ann. Surg., ii. 1885, p. 450. **Jessett** (Tumours of Neck): Med. Reg., Phila., 1887, p. 601; *Ibid.*, ii. pp. 1, 25, and 49. **Koplik** (Recent Contributions on): Ann. Surg., vi. 1887, p. 409. **Leopold** (Experimental): Arch. f. path. Anat., lxxxv. 1881, p. 283. **Lücke:** Pitha, Handbuch, ii. Ab. 1, 1869. **Moore** (Cancer, Tumours): Holmes' Surg., i. 1883. **Paget:** Lectures on Surg. Pathology (Ed. by Turner). **Phillips** (Congen. Sacral T.): Med. Times and Gaz., 1885, ii. p. 501. **Ping:** Contribution l'étude de l'hérédité d. tumeurs, 1885. **Renault** (Sacro-coccygian Tumour): Progrés méd., ii. 1885, p. 122. **Rosenberg:** Ueb. mediastinal. Tumoren bei Kindern, 1884. **Schaeffer** (Histological Changes in Muscle at Border of Tumours): Arch. f. path. Anat., cx. 1887, p. 443. **Schubert:** Ueb. mediastinaltumoren bei Kindern, 1887. **Senn:** Biology of Tumours, 1887. **Sutton (J. B.)** [Teratomata]: Journ. Comp. Med. and Surg., N. Y., viii. 1887, p. 295. **Virchow:** Die krankhaften Geschwülste, 1863-7; *also* (Metaplasia), Med. Times and Gaz., 1884, ii. p. 309. **Williams** (Vegetable Tumours, New Theory of Neoplasia): Trans. Path. Soc. Lond., xxxviii. 1887, p. 335. **Zahn:** Deut. Ztschr. f. Chir., xxii. 1885, p. 387.

CHAPTER XXX

THE BLOOD

PROPOSED DEFINITION.

336. VIRCHOW's definition of the blood as a "transitory tissue with fluid intercellular substance, permanently containing young tissue elements" (No. 13, ii. 1849, p. 592) is retained by many at the present day, and its diseases are often spoken about as those of a **fixed tissue**. There is reason to believe, however, as Osler remarks (No. 199, xxix. 1886, p. 377 *et seq.*), that this definition is somewhat unfortunate. A tissue has the power of reproducing itself from unlike materials supplied to it. The blood has not, and is dependent on different glands and gland-like structures for its maintenance and repair.

GENERAL CHARACTERS IN HEALTH.

337. It is an opaque, red, or dark purple-coloured liquid having a peculiar **odour**, and an average **specific gravity** of 1055, but oscillating within the bounds of health considerably above and below this.

Jones (No. 197, viii. No. 1, 1887), employing a modification of Roy's method of estimation (see Sect. 344), finds that the specific gravity is highest at birth (1066 in both sexes). It is at a minimum between the second week and the second year, and rises to a point attained in the male between the ages of thirty-five and forty-five. (1058·5), and in the female after the climacteric (1054·5). It tends to be higher in the male than in the female. The ingestion of mixed food causes a diminution, and exercise, if gentle and not too prolonged, has a like effect. With copious perspiration the specific gravity rises. During pregnancy it falls.

The colour of the blood in the new-born child is almost black, and although this diminishes as respiration is established, yet it continues to be dark blue coloured for several days after birth.

It is composed of a fluid part, the plasma or liquor sanguinis, and of particulate matter in the form of corpuscles suspended in this.

The **plasma** in Man is a clear, slightly straw-coloured liquid, having a specific gravity of 1026 to 1029, an *alkaline* reaction, and tending, when kept at a temperature a few degrees above freezing point, to precipitate fibrin.

The liquid which remains after the separation of the fibrin is the **serum**, and although, in the act of coagulation, certain solids have been thrown down from their previous state of solution, and a considerable number of its corpuscular elements (leucocytes and blood plates) have been destroyed, yet this does not materially influence the specific gravity, which still remains about 1028.

If separated from blood at a considerable interval after a meal, the serum is clear and limpid, but if a few hours only have elapsed, it presents some amount of milky turbidity. This is very apparent in some animals such as the cat, and is due to its containing a fine fatty emulsion.

The serum also has an *alkaline* reaction, more alkaline than the plasma from which it has been derived.

After the fibrinogen has been cast out in the act of coagulation, there still remain in the serum the following constituents :—

(*a*) Proteid matters.
(*b*) Extractives and fats.
(*c*) Salts.

The chief of the **proteids** are serum-globulin or para-globulin, and serum-albumin. The latter, according to Hammarsten (No. 169, 1878), is more abundant in human serum than in that of either the horse, ox, or rabbit.

The **extractives** are mainly kreatine, kreatinine, urea, uric acid, hippuric acid, succinic acid, xanthin, and hypoxanthin, but in healthy blood they are present only in very small quantity. Traces of grape sugar, sarcolactic acid, and indican are also found, and a yellow pigment gives the serum its characteristic colour. Cholesterine occurs in the dry residue in varying quantity.

The **neutral fats** are in great part triolein, tristearin, and tripalmitin.

Sodium chloride constitutes the chief ingredient of the **ash** in quantity varying from 61 to 65·2 per cent. The other **saline components** are sodic sulphate, carbonate, and phosphate, calcic phosphate, and magnesic phosphate.

Its Quantity.

338. In the case of Man there is always, of course, great difficulty in estimating this, and even in the lower animals, the results are probably only approximate. In Man it is generally reckoned as $\frac{1}{13}$ of the whole body weight. It amounts to less in childhood and in old age than in middle life.

339. **Methods of Estimating.**—Several have been suggested and put in use by Welcker (No 139, iv. 1858, p. 147), Malassez (No. 4, ii. 1875, p. 261), and others, all more or less unsatisfactory.

Grehant and Quinquad (No. 40, xciv. 1882, No. xxii.; and No. 200, xviii. 1882, p. 564) have devised a means, founded on the fact discovered by Claude Bernard, that carbonic oxide has the property of forming a compound with hæmoglobin more stable than that with its oxygen, which it consequently displaces. They start with a given amount of CO diluted with oxygen and hydrogen. The animal to be experimented upon is allowed to breathe this for about a quarter of an hour, and by comparing the amount of gas contained in a sample of blood withdrawn from the animal after this time with that which remains, and with that which has been expired or still remains in the air passages, they are able to form a pretty correct estimate by a simple calculation of the total quantity of blood. The method presupposes of course *that the CO combines equally* with the blood in all parts of the body, which they find to be the case.

Thus if 100 c.c. blood contain 8 c.c. CO, and if 64 c.c. CO have been absorbed, the blood volume will be expressed by:—

$$8 : 100 : 64 : x$$

They found in nine researches on dogs of different size that the total amount of blood was from $\frac{1}{13 \cdot 8}$ to $\frac{1}{11}$ of the body weight.

Its Corpuscles.

340. As previously mentioned (Sect. 144) they are of at least three kinds—*the coloured or hæmocytes, the colourless or leucocytes,* and *the blood plates or Hayem's hæmatoblasts.*

THE COLOURED CORPUSCLES.

341. **Structure.**—These are composed of an interlacing, sponge-like, albuminous stroma, whose spaces are filled with a faintly granular substance, the *hæmoglobin.* The stroma is hyaline, and is not colourable by staining reagents. It corresponds to the "*oikoid*" of Brücke. The contents of the stroma or "*zooid*" of Brücke, are capable of coloration. Ehrlich calls the stroma the "*discoplasma,*" and the contents he names the "*paraplasma.*"

Solution of Tannin was shown by Roberts (No. 9, July 1863, p. 70) to have the effect of causing a little homogeneous protrusion of the contents of the corpuscle from one side; and he also demonstrated that with solution of *Rosanilin nitrate* the corpuscles are rendered transparent, spherical, pale rose red, and, at one point in the periphery, there are sometimes seen two dark red spots either sunk in a hollow on the surface or projecting over it.

Rindfleisch (No. 201) called attention in the same year to some very remarkable phenomena which follow the application of *soluble aniline blue* to amphibian blood. The corpuscles become at first rounded and dark red. Suddenly, however, they

assume an unusual pallor and a mass is projected from one side which stains forthwith of a blue colour. The mass is divided into two layers—a central, which stains of a deep blue, and is homogeneous, the nucleus; and a peripheral, which becomes less deeply stained, and is finely granular. Several other aniline dyes appear to have the same action (Laptschinsky, No. 12, lxviii. iii. Ab. Jahrg. 1873, H. i.-v., 1874, p. 148).

In Man, the coloured corpuscles do not possess a nucleus nor have they any boundary membrane.

Boettcher (No. 13, xxxvi. 1886, p. 342) was of opinion that the coloured corpuscles, in the higher mammals, had a shrunken rudimentary nucleus. They contain about 50 per cent of water, and the main solid component is hæmoglobin (C 53·85, H 7·32, N 16·17, Fe 0·42, S 0·39), the substance which imparts to them their colour.

Hæmoglobin seems to be a compound of hæmatin (containing the iron) and a proteid substance closely related to, if not identical with, globulin.

Potash salts and phosphates preponderate in the *corpuscles*, while *soda salts*, and more especially *chlorides*, prevail in the serum.

As the corpuscles form the chief solid constituent of the blood, and as they are, for the most part, composed of *hæmoglobin*, it is impossible to overrate the importance of this substance in almost all the diseases of the blood.

342. **Size.**—The size of the corpuscles in health is a matter which requires to be very carefully investigated before studying the diseases of the blood.

The *breadth* of the coloured, according to Gulliver, is approximately 7·9 μ ($\frac{1}{3500}$ to $\frac{1}{3200}$ of an inch), and their thickness may be taken as equivalent to about 1·8 μ ($\frac{1}{12400}$ of an inch), but some have a diameter of only 6·5 μ while others may reach 8·5 μ.

Osler calculates that those of medium size comprise about 75 per cent of the whole, and the largest and smallest about 12 per cent each. In the *new born*, and for some time after birth, the maximum and minimum size of the corpuscles has a much wider range (10·3 to 3·3 μ). One of the most striking alterations in disease is the reversion to this fœtal state. To the smallest corpuscles (2·5 to 3·5 μ) the name of **microcytes** has been given, while those which are unusually large (8·5 up to 10, 12, or 14 μ) have been designated **megalocytes.**

Gram (No. 11, ii. 1884, p. 47) gives the size of the coloured corpuscles in health as ranging between 9·3 and 6·7 μ, and states that, on an average, the most of them are from 8·0 to 7·7 μ. He draws attention to a curious fact, namely, that the further north one proceeds the larger the diameter of the corpuscles in the inhabitants becomes. He quotes the undernoted in four different nations:—

Italians	7·0-7·5 μ.
French	7·5-7·6 μ.
Germans	7·8 μ.
Norwegians . . .	8·5 μ.

343. **The number** of coloured corpuscles per cubic millimètre of blood in a middle-aged male, is generally considered to be about 5,000,000. In the female it is somewhat less. Bouchut and Dubrisay

(No. 204, xiv. and xv. 1878; No. 49, 1878, i. p. 217) give the following quotations for different ages :—

Age.	Red blood-corpuscles.	Colourless blood-corpuscles.	Relationship of colourless to coloured.
From 2½ to 5 years . .	4,269,911	6704	1:648
From 20 to 30 years . .	4,192,687	6113	1:700
From 30 to 56 years . .	4,080,113	6931	1:616

In childhood, there is no difference as regards sex, but, in adult life, the coloured are fewer in women than in men.

344. **The specific gravity** of the blood corpuscles is said to be 1105, and as that of the plasma is regarded as being somewhat less, (1027), the corpuscles tend to sink if coagulation is prevented. The specific gravity of the colourless, as previously explained (Sect. 156), must be considerably less, although never exactly determined in healthy blood.[1]

The above statement in reference to the relationship of the specific gravities of the coloured corpuscles and plasma is that which is usually accepted. There is grave doubt, however, whether it be correct. The blood is such an unstable compound that observations made on the specific gravity of the plasma and corpuscles in blood which has been shed more than a few moments, must necessarily be untrustworthy. No one can peruse the account of the beautiful researches of Hayem and Bizzozero on the coagulation of the blood without feeling that all such observations must be made on blood within the vessels, or with apparatus that will supply corresponding physical conditions.

Roy (No. 216, i. 1883, p. 561; also No. 285, March 1884) has attempted to get over the difficulty in the following manner: A drop of the blood is introduced into a mixture of glycerine and water of known specific gravity, and notice is taken of whether it sinks or swims. By having a large selection of such solutions one is found in which the blood remains neutral. The specific gravity of this being known, indicates, of course, that of the blood.

The extreme instability in composition of the blood was long ago pointed out by Hewson (No. 230, p. 42) and illustrated by many experiments. Referring to the fact that in blood-letting the first evacuation of blood sometimes has an inflammatory crust, while the last has none, he concludes with the following sentence. "I therefore suspect that in such cases the properties of the blood are changed, even during the time of evacuation."

Literature on Specific Gravity of Blood.—**Davy**: Ed. M. and S. J., xxix. 1828, p. 244. **Jurin**: Phil. Trans., Lond., v. 1700-20, p. 320. **E. Jones Lloyd** (Variations in Health): Journ. Physiol., Camb., viii. No. 1, 1887. **Roy** (Method of Measuring): Ed. Clin. and Path. J., i. 1883, p. 561.

THE COLOURLESS CORPUSCLES.

345. These are granular masses of protoplasm containing one, two, or more nuclei, and having the power of amœboid movement. In human blood they are, as a rule, larger than the coloured corpuscles, but are not all of the same size.

[1] For further details regarding the relationship of the specific gravity of the corpuscles to that of the plasma and serum, the reader is referred to Hewson's Works (No. 230) and to Gulliver's Essay (No. 19, lxiv. 1845, p. 360).

Max Schultze, several years ago, showed that the leucocytes circulating in the blood could be classified into several anatomical groups. He distinguished (1) such as are smaller than a coloured corpuscle, which are round in shape, and whose protoplasm is scanty; (2) those which are round, but which are about the size of a coloured corpuscle; and (3) the large cells with abundant protoplasm, and whose amœboid movements are very evident.

Ehrlich (No. 91, i. 1880, p. 554) has demonstrated that it is possible to distinguish five different kinds of leucocyte according to the reaction of the granules within them to aniline dyes; and he accordingly designates them "α," "β," etc., up to "ϵ" leucocytes.

Some of the granules stain in *acid* aniline dyes, others in *basic;* while a third set is colourable with those which are *neutral.* Those stainable in acid dyes are met with in a small number of the leucocytes in *normal* human blood; while those which are sensitive to the basic dyes are mostly found in *leucocythæmic* blood. The majority of the leucocytes found in normal human blood are affected by those which are neutral. *Pus cells* correspond, as regards their powers of staining, with the leucocytes of the blood.

The granules contained in the leucocytes also differ from each other in respect of their solubility in different reagents, their size, form, refraction, behaviour under high temperatures, and distribution in the cell body. He also finds that the granules of the "β" leucocytes stain black with *Indulin.*

He dries the blood on a cover-slip and afterwards stains it.

Bizzozero (No. 4, May and August 1879, Nos. 3 and 4, p. 201) distinguishes four kinds of leucocyte according to their size, nucleation, etc. In Nos. 1 and 2 the nucleus is single, in No. 3 there are from two to five, and in No. 4 it is single, double, or dividing.

Heyl (*Dissertation*, Dorpat, 1882; No. 11, i. 1883, p. 406) divides the leucocytes into two kinds according as they disappear during coagulation or not. He distinguishes the former as "α," the latter as "β" leucocytes.

THE HÆMATOBLASTS (HAYEM) OR BLOOD PLATES (BIZZOZERO).

346. These have already been described (Sect. 145), and it only remains to remind the reader that they must not be mistaken for **Neumann's hæmatoblasts** found in bone marrow, and frequently referred to further on.

Halla (No. 141, 1883, p. 198) finds that the hæmatoblasts are reduced in number in continued fever, typhoid, and pernicious anæmia; while at the end of pregnancy, in pulmonary tuberculosis, and in inflammatory conditions, they are often so abundant that they become collected into ball-like masses. He cannot doubt their connection with the process of coagulation.

REACTION.

METHODS OF TESTING.

347. Owing to the blood being of such an opaque red colour, ordinary methods of testing the reaction are unsuitable when applied to it. In order to overcome this difficulty various ingenious devices have been employed by Kühne, Liebreich, Zuntz, Schäfer, and others.

Liebreich's Method (No. 227, 1868, p. 48).—Small plates of plaster of Paris of neutral reaction are prepared. After being cast and dried they are coloured with neutral litmus. A drop of the blood to be tested is allowed to fall upon a plaster plate. The dry plaster readily absorbs the liquid and leaves the corpuscles on the surface. If the latter be washed off in a stream of water, the reaction will be indicated on the spot where the blood has lain.

Schäfer's Method (No. 179, iii. p. 292).—A drop of the blood is allowed to fall on glazed paper slightly coloured with red litmus. On wiping it off, after a few seconds, the reaction will be indicated.[1]

De Renzi (No. 13, cii. 1885, p. 218) employs thin neutral gypsum plates, but allows the blood to fall on one side, and tests the reaction on the opposite with litmus paper.

REACTION IN DISEASE.

348. The normal reaction of the blood is alkaline, but it is said to possess an acid reaction in **leucocythæmia** (Scherer, No. 13, v. 1864, p. 51; Pettenkofer and Voit, No. 228, v. p. 320, and others). It is questionable, however, whether this statement can be relied upon, many of the observations being faulty from having been made after death, or from some other cause.

De Renzi (*loc. cit.*) found that in 2 cases out of 59 patients suffering from various diseases, the reaction was acid (catarrhal icterus and suppurative hepatitis); in 20 cases it was very weakly alkaline; in 19 weakly alkaline; and in 16 strongly alkaline. Its alkalinity increased by the consumption of **alkaline carbonates, Karlsbad water,** and **salicylate of soda. Hydrochloric acid** diminished it. After death it gradually lost its acid reaction.

Literature on Reaction of Blood.—**Gamgee**: Physiological Chemistry, 1880, p. 26. **Gscheidlen**: Physiologische Methodik, p. 324 *et seq.* **Kühne**: Arch. f. path. Anat., xxxiii. 1865, p. 95. **Lassar**: Arch. f. d. ges. Physiol., ix. 1874, p. 44. **De Renzi**: Arch. f. path. Anat., cii. 1885, p. 218. **Schäfer**: Journ. of Physiol. Camb., iii. p. 292. **Zuntz**: Centralbl. f. d. med. Wissensch., 1867, p. 34.

ESTIMATION OF THE HÆMOGLOBIN.

349. The methods may be divided into those which are founded upon chemical analysis and those which are chromometric in their nature—that is to say, in which the colour of the blood is compared with *certain standard colour tests.* The old methods belonged almost entirely to the former class, but of late, they have been in great part superseded by those which are colorimetric.

(1) *CHEMICAL.*

350. **By the Estimation of the Iron.**—This is one of the best known. It is based upon the fact that all the iron of the blood is con-

[1] This paper can be had from Messrs. Tounson & Mercer, Bishopsgate Street, London.

tained in the hæmoglobin, that it is equally distributed, and that it is present in constant proportion. Hence, if the quantity of iron in a sample of blood is known, the corresponding amount of hæmoglobin can be readily arrived at.

Other chemical methods, founded upon the estimation of the **oxygen** contained in the blood (Quinquad, No. 214, p. 33), or on the calculation of the amount of **hæmatin** (referred to by Malassez, No. 4, iv. 1877, p. 4), have also been devised and put in practice, but all are more or less inconvenient, owing to the fact that they are lengthy and complicated, and that a considerable mass of blood is necessary for their accomplishment.

(2) *COLORIMETRIC.*

351. The colorimetric methods are much more easily carried out, and have been found in clinical use to yield results sufficiently accurate to afford very valuable information.

Malassez (*loc. cit.*) divides them into two sets.

In the former, the sample of blood to be examined is diluted with water until it agrees in colour with a standard coloured solution whose tint has previously been determined to correspond to a certain richness in Hb.

The principle involved in this system is alike with that in the methods of Hoppe-Seyler (No. 30, p. 385), and of Preyer (No. 20, cxl. p. 187).

In the latter, the dilution of the blood is always carried to the same point, and the tint is compared with a standard scale of colours equivalent in intensity to blood containing known strengths of Hb. Such are the systems of Welcker (No. 221, xliv. 1854, p. 11) and of Hayem (No. 40, July 10, 1876; No. 218, p. 47).

352. In **Hoppe-Seyler's Method** a solution of oxyhæmoglobin of known strength is placed in a hæmatinometer. The hæmatinometer consists of a flat vessel whose sides are one ctm. apart. In a similar hæmatinometer is placed the blood to be examined, defibrinated and diluted to a known extent. On comparing the two, it will probably be found that the colour of the blood is much deeper than that of the solution of hæmoglobin. Water is now added to the blood from a graduated burette until the two colours correspond. By a simple calculation of the amount of water required to accomplish this, the quantity of hæmoglobin in the blood may be determined.

Preyer's Method is based upon the fact that if a solution of oxyhæmoglobin be placed in the hæmatinometer (see above), and examined spectroscopically, only the red rays will pass if the solution be very strong. If, however, the solution be diluted, there comes a time when the green rays are also rendered visible. The corresponding strength of hæmoglobin solution, when they first come into view, is then calculated.

In actually estimating the quantity of Hb in a sample of blood, a measured quantity of defibrinated blood (5 to 8 c.c.) is placed in the hæmatinometer. It is now diluted with water from a burette just until the green rays become visible. By reading off the amount of water necessary to effect this, and comparing the result

with a solution of oxyhæmoglobin of known strength, which will also just permit the green rays to pass, the quantity of Hb in the sample of blood can be ascertained.

353. **Malassez' Method.**—Both of these methods require pure oxyhæmoglobin, and as this substance is procurable with difficulty, there must always be a manifest objection to their use. It was found by Malassez (*loc. cit.*, p. 19) that, where the estimation of hæmoglobin implies a mere comparison of tints, picrocarminate of ammonia can be substituted with equal efficiency. The picrocarminate solution must of course be made in a particular manner (*loc. cit.*, p. 21), and is placed in a movable prism, which, by being viewed at its edge or through a greater thickness, presents degrees of colour which have been previously ascertained to correspond to certain strengths of oxyhæmoglobin. The sample of blood, in a known state of dilution, is placed side by side with the coloured prism, and the latter is moved along by means of a screw until the two correspond. An index affords evidence of the amount of colouring matter in the sample of blood, according to the distance through which the prism has moved. The details of the apparatus are the following:—

354. **Malassez' Hæmochromometer.**—The apparatus (No. 4, iv. 1877, p. 19) consists of a rectangular screen 36 ctm. long by 20 ctm. high. It is pierced towards its centre by two holes 5 mm. in diameter. These holes are placed close together and in the same horizontal line.

Behind one of the two holes (the left) is placed a Potain's mixer (see Sect. 358) whose reservoir, instead of being circular, is made flat on two sides, so that a uniformly thick stratum of blood may be examined. The two sides are separated in all these mixers for an equal distance (5 mm.).

The mixer is held applied against the screen by means of an elastic band under which its long end is passed.

Behind the other aperture of the screen is placed the prism filled with the picrocarminate solution. It is fixed on a wagon moved by means of a rack; and when made to ascend or descend, various degrees of thickness of the colouring fluid are of course brought into view. By this means, the exact point where the two colours correspond can be discovered. A small needle in connection with the prism indicates on a scale the number of degrees which have been traversed. Behind the mixer and the prism is a piece of ground glass for the purpose of diffusing the light.

A table accompanies the apparatus, indicating the value of each degree in Hb per cu. mm., together with the corresponding respiratory capacity or ability to absorb oxygen. The divisions on the scale have been established experimentally, the respiratory capacity by means of the mercurial pump.

The first row of figures on the table contains the numbers on the colorimetric scale; the second, the respiratory capacities expressed in volume; and the third, the richness of Hb expressed in weight per cu. mm. of blood. From the fact of the calculation being for a cu. mm., the richness in Hb can be readily contrasted with the number of blood corpuscles, which is also usually expressed as per cu. mm.

Method of Procedure.—(1) Make a one per cent mixture of blood by means of the mixer. This is done as in diluting the blood for counting the number of corpuscles (see Sect. 358), only, distilled water is used instead of serum. Prick the end of the finger with a pin, needle, or the point of a lancet, and press out the blood. Aspirate the blood into the long end of the mixer until it meets the mark 1. Aspirate the water into the reservoir immediately afterwards up to the mark 100. Shake the tube so as to thoroughly mix the two.

(2) Fix the mixer on the screen, taking care that the reservoir corresponds in position to the aperture.

(3) Find out the position of the prism which gives a colour of the same strength

as that of the solution of blood. The direct rays of the sun and a blue sky should be avoided in determining this. The light ought to be taken, if possible, from a window giving a clear diffuse light reflected from a white background.

(4) Note the degree on the scale that the needle stands opposite, and compare it with the table before referred to. If the blood is so poor that the figure sinks beyond the limits of the scale, make a two per cent mixture by filling the long end of the mixer twice, an operation which is easily accomplished if care be observed to interpose a globule of air between the first and second parts taken. In calculating the result, divide the figures given in the table corresponding to the degree indicated by the needle on the scale, by 2.

If, on the contrary, the blood is too rich, the opposite limits of the scale would be passed. To avoid this, make a half per cent mixture and double the resulting quantities.

355. **Gowers' Hæmoglobinometer** (No. 368, xii. 1879, p. 64).

FIG. 175.—GOWERS' HÆMOGLOBINOMETER.

(A) Bottle with pipette stopper for holding the diluting solution; (B) capillary pipette for measuring the blood; (C) graduated tube for measuring the amount of hæmoglobin; (D) standard tint of normal blood; (E) support for D and C; (F) puncturing needle.

"The tint of the dilution of a given volume of blood with distilled water is taken as the index to the amount of hæmoglobin. The distilled water rapidly dissolves out all the hæmoglobin, as is shown by the fact that the tint of the dilution undergoes no change on standing. The colour of a dilution of average normal blood one hundred times is taken as the standard. The quantity of hæmoglobin is indicated by the amount of distilled water needed to obtain the tint with the same volume of blood under examination as was taken of the standard. On account of the instability of a standard dilution of blood, tinted glycerine-jelly is employed instead. This is perfectly stable, and by means of carmine and picro-carmine the exact tint of diluted blood can be obtained.

"The apparatus consists of two glass tubes of exactly the same size. One contains a standard of the tint of a dilution of 20 cubic mm. of blood, in 2 cubic centimetres of water (1 in 100).

"The second tube is graduated, 100 degrees = 2 centimetres (100 times 20 cubic millimetres).

"The 20 cubic millimetres of blood are measured by a capillary pipette (similar to, but larger than that used for the hæmacytometer). This quantity of the blood to be tested is ejected into the bottom of the tube, a few drops of distilled water being first placed in the latter. The mixture is rapidly agitated to prevent the coagulation of the blood. The distilled water is then added drop by drop (from the pipette stopper of a bottle supplied for that purpose) until the tint of the dilution is the same as that of the standard, and the amount of water which has been added (i.e. the degrees of dilution) indicates the amount of hæmoglobin.

"Since average normal blood yields the tint of the standard at 100 degrees of dilution, the number of degrees of dilution necessary to obtain the same tint with a given specimen of blood is the per centage proportion of the hæmoglobin contained in it, compared to the normal.

"For instance, the 20 cubic millimetres of blood from a patient with anæmia gave the standard tint at 30 degrees of dilution. Hence it contained only 30 per cent of the normal quantity of hæmoglobin.

"By ascertaining with the hæmacytometer the corpuscular richness of the blood, we are able to compare the two. A fraction, of which the numerator is the per centage of hæmoglobin, and the denominator the percentage of corpuscles, gives at once the average value per corpuscle. Thus, the blood mentioned above containing 30 per cent of hæmoglobin, contained 60 per cent of corpuscles; hence the average value of each corpuscle was $\frac{30}{60}$ or $\frac{1}{2}$ of the normal. Variations in the amount of hæmoglobin may be recorded on the same chart as that employed for the corpuscles.

"In using the instrument the tint may be estimated by holding the tubes between the eye and a window, or by placing a piece of white paper behind the tubes; the former is perhaps the best. Care must be taken that the tubes are always held in the line of light, not below it. In the latter case some light is reflected from the suspended corpuscles from which the hæmoglobin has been dissolved. If the value of the corpuscles is small then a perceptibly paler tint is seen when the tubes are held below the line of illumination. If all the light is transmitted directly through the tubes, the corpuscles do not interfere with the tint.

"In using the instrument it will be found that during six or eight degrees of dilution it is difficult to distinguish a difference between the tint of the tubes. It is therefore necessary to note the degree at which the colour of the dilution ceases to be deeper than the standard, and also that at which it is distinctly paler. The degree midway between these two will represent the hæmoglobin percentage.

"The instrument is only expected to yield approximate results, accurate within two or three per cent. It has, however, been found of much utility in clinical observation."

Literature on Estimation of Hæmoglobin.—**v. Fleischl** (Hæmometer): Wien med. Bl., ix. 1886, p. 268. **v. Fleischl and v. Marscow:** Med. Jahrb., Wien., i. 1886, p. 167. **Hüfner:** Ztscher. f. physiol. Chem., iii. 1879, p. 1. **Laker:** Wien. med. Wochnschr., xxxvi. 1886, p. 639 *et seq.* **Liman:** Centralbl. f. d. med. Wissensch., xiv. 1876, p. 353. **Malassez:** Arch. de physiol., iv. 1877, p. 634. **Müller:** Arch. f. wissensch. u. prakt. Thierh., xii. 1886, p. 97. **Welcker:** Zeitschr. f. rat. med., iv. 1858.

Hæmoglobin in Disease.

356. According to Fenoglio (No. 237, 1880; No. 49, i. 1880, p. 240), the colour of the face and mucous membranes is not always an indication of a want or of an abundance of hæmoglobin.

In the following diseases the quantity of hæmoglobin is diminished: Anæmia from hæmorrhage, chlorosis, pernicious anæmia, the anæmia of

organic disease of the stomach; in leucocythæmia, Hodgkin's disease, Bright's disease, typhoid fever, the later stages of pneumonia (Fenoglio), pulmonary phthisis, in valvular disease of the heart, unless where there is great cyanosis, and cirrhosis of the liver (Quincke and Fenoglio). The greatest depreciation in the quantity found by Fenoglio was in a workman in the St. Gothard tunnel affected with the duodenal blood-sucking parasite, the *anchylostoma duodenale.*

In chlorosis, leucocythæmia, pernicious anæmia, and Hodgkin's disease it may fall 70 per cent or even more.

In variola and typhoid it is diminished. During the desquamative stage of scarlatina, in previously healthy children, there is an addition to the quantity of hæmoglobin and to the number of corpuscles (Arnheim).

General Literature on Hæmoglobin.—**Addison**: Brit. M. Journ., 1864, i. pp. 202. 282. **Bernard (C.)**: J. de la Physiol. de l'homme, i. 1858, p. 233; *Ibid.*, i. 1858, p. 649; *also*, Compt. rend. Acad. d. Sc., xlvii. 1858, p. 245. **Bizzozero** (Chromo-cytometer): Gaz. méd. de Par., 1879, p. 634. **Bollinger**: Deut. Zeitschr. f. Thiermed., iii. **Christison**: Ed. Med. and Surg. Journ., xxxv. 1831, p. 94. **Cutler and Bradford**: J. of Physiol., Camb., i. 1879, p. 427. **Ehrlich**: Deut. med. Wochnschr., xvi. 1881. **Hayem**: Compt. rend. Soc. d. Biol., iii. 1877, p. 316; *also* (Methæmoglobin), Rev. scient., xxxvii. 1886, p. 717. **Leichtenstern**: Untersuchungen üb. d. Hæmoglobulingehalt d. Blutes in gesunden u. kranken Zuständen, 1878. **Lichtheim**: Samm. klin. Vorträge, xi. (Inn. Med.), p. 1147, No. 134. **MacMunn**: Quart. J. Mic. Sc., xxv. 1885, p. 469. **Malassez** (Colorimeter): Compt. rend. Soc. de Biol., iii. 1877, p. 309; *also*, Compt. rend. Acad. d. Sc., lxxxv. 1877, p. 348; *also* Arch. de Physiol., iv. 1877, pp. 1 and 634. **Nencki** (Parahæmoglobin): Arch. f. exper. Path. u. Pharmakol., xx. 1885, p. 332. **Preyer**: Centralbl. f. d. med. Wissensch., v. 1867, pp. 259, 273. **Quinke**: Arch. f. path. Anat., liv. 1872, p. 537; *also* (Hæmochromometer), Berl. klin. Wochnschr., xv. 1878, p. 473. **Sanderson**: Med. Times and Gaz., 1871, i. p. 211. **Silbermann**: Breslau Aerztl. Ztschr., viii. 1886, p. 183. **Subbotin** (Influence of Nourishment on): Zeitschr. f. Biol., München, vii. 1871, p. 185. **Vierordt**: Arch. f. d. ges. Physiol., ii. 1869, p. 178. **Worm-Müller** (Relation between Corpuscles and Colour of Blood): (Abstr.) Maly's Jahresbericht, vii. 1878, p. 102.

NUMERATION OF CORPUSCLES.

357. The instruments which have been devised for this purpose are numerous, but the principle involved in them is alike. It consists in diluting a known quantity of blood up to a given point and subsequently counting the number contained in a certain known bulk.

The method suggested by Vierordt (No. 138, xi. pp. 26, 327, 854; xiii. p. 259) and carried out by Welcker (No. 139, xx.; No. 75, Rollet, article "Blood") was one of the earliest, but as it has now been superseded by methods of greater accuracy and of more easy application, it need not be further described at present.

MALASSEZ' METHOD.

358. By means of Malassez' instrument (No. 40, Dec. 1872) results of great accuracy can be attained, but it is questionable whether reliance can be placed upon it so much as upon that of Hayem or Nachet, or Gower's modification of the same. The fact that the blood has to run

along a tube, tends to distribute the blood corpuscles unequally. It is also more inconvenient than the above, from its requiring a quadrilled eye-piece.

Procedure.—Make a standard mixture of blood and artificial serum (1 to 100), the serum[1] (Potain and Malassez) being composed of—

1 vol. solution gum acacia, density 1020.
3 vols. equal parts sulphate of soda and chloride of sodium, each having a density of 1020.

Mix the blood and serum in a Potain's mixer. The Potain's mixer is composed of a fine capillary tube, having an ampullary dilatation or reservoir a little beyond its middle. It is, in fact, a pipette with a bulb in its course. The short part of the tube has a bore a little larger than the long, and to it a piece of caoutchouc tubing

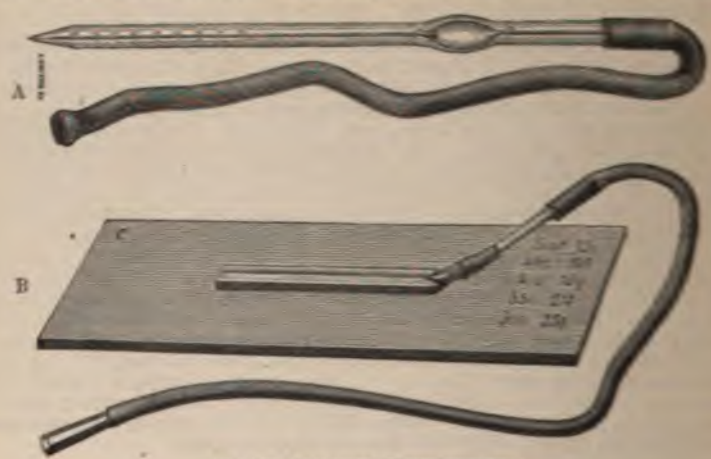

FIG. 176.—MALASSEZ' HÆMOCYTOMETER.
A, the Potain's mixer. B, the artificial capillary.

is attached. The reservoir has a small glass bead in its interior, and the long end of the instrument comes to a finely-tapered point. The apparatus is so constructed that the long part of the tube is exactly the $\frac{1}{101}$th part capacity of the reservoir. A line at each extremity of the reservoir marks off the limits. Another line placed on the long end of the tube divides it into two parts of equal capacity.

Dip the point of the instrument into the blood obtained by pricking the end of the finger, and aspirate through the caoutchouc tube, just until the blood rises to the line which separates the long portion of the tube from the ampullary dilatation. If the blood has run beyond this point, blow a little out. The aspiration of the blood must be done quickly, as the latter tends to coagulate.

Dry the point of the instrument, and dip it into the artificial serum, aspirating anew. Rotate the tube while aspirating, in order to mix the contents, and continue to aspirate until the reservoir is filled to the line at its upper extremity. Shake the apparatus so that the little bead in the reservoir is set in motion. By this means the mixing will be aided.

[1] In a later article Malassez states that he prefers a 5 to 6 per cent solution of non-deliquescent sodic sulphate.

The liquid within the reservoir now contains 1 per cent of blood. If a mixture of 1 to 200 is required, the blood is aspirated up to the line in the middle of the long end of the instrument. Such a strength ought to be employed when the number of corpuscles rises above 2,000,000 per cu. mm., and the 1 to 100 mixture when below this.

The mixture having been made, it is introduced into a fine specially-prepared capillary tube called **the artificial capillary.** This is from 2 to 3 centimètres long, has a bore of from 4 to 5 mm., a thickness of 1 mm., and is fixed on a stand. It is flattened from above downwards, and the bore is so narrow that it can hardly be seen with the naked eye. On section, it forms an ellipse whose long axis measures about 250 μ, and its small 70 μ. One of its extremities is free; the other, considerably thicker, is attached to a piece of caoutchouc tubing. Its capacities have been previously

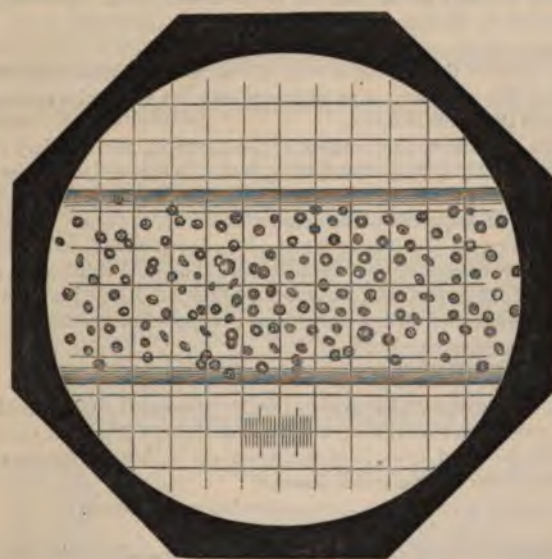

FIG. 177.—MALASSEZ' HÆMOCYTOMETER.
The appearance of the artificial capillary when seen microscopically.

accurately ascertained, and the figures engraved on the side of the stand indicate what these are for given lengths of the tube. In the column to the left are inscribed the lengths, and in that to the right the ascertained capacities. The lengths are expressed in thousandths of a millimètre, the capacities in fractions of a cubic millimètre. The capillary represented in the illustration, for instance, has a capacity equal to the 150th part of a cu. mm. for a length of 500 μ.

The capillary is filled by placing a drop of the mixed blood at its end, and aspirating if necessary. The liquid which first flows out of the mixer ought to be rejected. The tube should be filled quickly, as by that means the corpuscles are more equally disseminated. It is often sufficient to allow the blood to ascend the tube by capillarity, but if it runs too slowly, it must be aspirated. When the tube is nearly filled, remove the remainder with blotting-paper.

An eye-piece micrometer must now be procured, and the value of the length of one side of the mass of squares in it ascertained, so that when a piece of the tube

corresponding to a side of the mass of squares filled with the blood, is under observation, its length may be known. This is accomplished by a stage micrometer divided into 100ths of a mm. Each division, therefore, corresponds to 10 μ (μ = 1000 part of 1 mm.). Take any of the lengths of tube engraved on the side of the instrument, whose cubic capacity has been previously fixed. In the drawing given they are 300, 350, 400, 450, and 500 μ, and their capacities are respectively $\frac{1}{150}$, $\frac{1}{125}$, $\frac{1}{100}$, $\frac{1}{75}$ and $\frac{1}{50}$th of a cu. mm.

Let the length fixed upon be 500 μ. Draw out the upper tube of the microscope until one side of the mass of squares corresponds to 500 μ on the stage micrometer. With this amount of withdrawal of the upper tube, therefore, the length of the mass of squares from side to side will correspond to 500 μ of the tube when it is under observation. It is well to mark on the microscope tube the extent to which it has been drawn out, and to use this for future observations. The capillary is now placed in position on the microscope stage, when the appearance shown in Fig. 177 will be seen.

Count the whole of the corpuscles in all the squares; and make the numeration at several parts of the capillary, so as to ensure that the corpuscles are equally distributed, and take the mean number.

Calculation.—Multiply this number by the figure on the capillary stand which represents the capacity of the particular length of tube through which the numeration has been made and by the figure representing the dilution of the blood. The product gives the number of corpuscles per cu. mm. of blood.

Example.—Suppose that 118 be the number of corpuscles found in 500 μ length of tube. Suppose, further, that in the particular tube used this length represents a cubic capacity of 150th part of a millimètre. Suppose, lastly, that the dilution of the blood has been carried to 1 in 200. The number of corpuscles per cu. mm. of blood will then be represented by

$$118 \times 150 \times 200 = 3{,}540{,}000.$$

After each examination the apparatus should be emptied, and cleaned by aspirating distilled water into the capillary and blowing it out. Wash out the mixer in the same way. If the blood dries in either, wash out with a 25 per cent solution of potash or soda, followed by distilled water.

In order to avoid error, repeat the examination several times.

359. **Numeration of the Leucocytes.**—Less dilution is necessary. Take a 1 to 50 solution. Make it by drawing up a tubeful of blood, followed by a second tubeful, but with a globule of air between them so as to mark off the one from the other, and mix as before. As the leucocytes are sparsely distributed, they must be counted throughout a greater length of tube than previously, so that if the quadrated field covers $\frac{1}{2}$ mm. (500 μ) of the capillary, it will be necessary to observe the fields through $\frac{1}{2}$ to 1 ctm. of its length.

Thoma (quoted by Landois) recommends the addition of 10 parts of 0·5 per cent solution of acetic acid, which destroys all the coloured corpuscles.

Calculation.—Suppose that, on examining twenty microscopic fields, thirty-two colourless corpuscles have been found, then the corpuscular value of each length of the tube observed is $\frac{32}{20} = 1{\cdot}6$. Suppose that each length of the tube taken represents a distance of 500 μ, and that the distance in the tube in use corresponds to a cubic capacity

of $\frac{1}{100}$th cu. mm., the number of colourless globules per cubic millimètre of blood will then be

$$1{\cdot}6 \times 100 \times 50 \text{ (the extent of the dilution)} = 8000.$$

GOWERS' HÆMACYTOMETER.

360. This, as before stated, is essentially a modification of Hayem and Nachet's instrument. The results obtainable by it are wonderfully accurate, if sufficient observations are made by *the same* observer. It is the instrument in general use in this country. Dr. Gowers' description of it (No. 59, 1877, ii. p. 797) is the following:—

FIG. 178.—GOWERS' HÆMACYTOMETER.

A, pipette for measuring diluting solution; B, capillary tube for measuring blood; C, the cell; D, small glass jar for making the dilution; E, a small spoon for mixing; F, needle for puncturing the finger.

"The hæmacytometer consists of (1) a small pipette, holding exactly 995 cubic millimètres; (2) a fine capillary tube holding five cubic millimètres; (3) a small glass jar, in which the dilution is made; (4) the cell exactly $\frac{1}{5}$ of a millimètre deep, the floor of which is ruled in tenth of a millimètre squares.

"**Various diluting solutions** have been recommended, in order to change as little as possible the aspect of the corpuscles. It is not well, however, to endeavour to observe the characters of the corpuscles during the numeration; whatever solution is employed, the corpuscles are more or less changed by it. One which answers very well is a solution of sulphate of soda of a specific gravity of 1025.[1]

[1] In a later note on the subject (No 59, 1878, ii. p. 901) Dr. Gowers recommends a mixture of sulphate of soda 104 grains, acetic acid 1 dr., and distilled water 4 oz. He says it renders the coloured more uniform in aspect, and the colourless more distinct.

"**The mode of proceeding** is extremely simple. A pipetteful of the solution is placed in the mixing vessel. Five cubic millimètres of blood are drawn into the capillary tube from a drop in the finger, and then blown out into the solution. The two are well mixed by a glass rod; a drop of the dilution is placed in the centre of the cell; the covering glass is applied and secured by the springs, and the slide placed on the stage of the microscope. The lens is then focussed to the squares. In a few minutes the corpuscles have sunk on to the squares. The number in ten squares is counted, and this, multiplied by 10,000, gives the number in a cubic millimètre of blood. . . . The number per cubic millimètre is the common mode of stating the corpuscular richness of the blood. But by employing this dilution, and squares of this size, a much more convenient mode of statement is obtained. Taking five millions as the average per cubic millimètre in healthy blood, the average number in two squares of the cell is 100. The number in two squares (ascertained by counting a large number, ten or twenty, and taking the mean) thus expresses the **percentage proportion** of the corpuscles to that of health, or, made into a two-place decimal, the proportion which the corpuscular richness of the blood examined bears to healthy blood taken as unity, or the number in twenty squares may be taken as a three-place decimal."

Literature on Numeration of Blood Corpuscles in Health and Disease. — **Amory:** Boston M. and S. Journ., 1879, p. 555. **Bouchut et Dubrisay:** Gaz. méd. de Paris, vii. 1878, pp. 168, 178. **Foa and Pellacani:** Spalanzani, Modena, ix. 1880, p. 16. **Gowers:** Lancet, 1877, ii. p. 797; *also*, Practitioner, xx. 1878, p. 1. **Grancher:** Compt. rend. Soc. de Biol., iii. 1877, p. 192. **Hayem:** Gaz. heb. de méd., xii. 1875, p. 291. **Hayem and Nachet** (Apparatus for): Lond. Med. Rec., iii. 1875, p. 457. **Henry and Nancrede:** Boston M. and S. Journ., 1879, p. 489. **Hirt:** Arch. f. Anat. Physiol. u. wissensch. Med., 1856, p. 174. **Keyes** (Effects of Mercury): Am. J. Med. Sc., lxxi. 1876. p. 17. **Kurz:** Berl. klin. Wochnschr., xv. 1878, p. 193. **Laptschinski** (in Relapsing Fever): Centralbl. f. d. med. Wissensch., xiii. 1875, p. 36. **Lemmon:** Virginia Med. Monthly, Richmond, v. 1878, p. 871. **Lyon:** Arch. f. path. Anat., lxxxiv. 1881, p. 207. **Malassez:** De la Numération des globules rouges du sang, 1873; *also*, Compt. rend. Soc. de Biol., 1875, p. 333; *also*, Arch. de physiol. norm. et path., i. 1874, p. 32; *Ibid.*, vii. 1880, p. 377. **Patrigeon:** Recherches sur le nombre des globules rouges et blancs du sang, etc., 1877. **Siegel:** Allg. Wien. Med. Ztng., xxix. 1884, pp. 127, 173, 272. **Stöltzing:** Ueb. Zählung der Blutkörperchen, 1856. **Thin** (in Skin Diseases): Med. Chir. Trans., Lond., lxi. 1878, p. 95. **Thoma:** Arch. f. path. Anat., lxxxvii. 1882, p. 201. **Toison:** Sur la numération des éléments du sang, 1885. **Tonassier:** De la numération des Globules du sang, etc. 1876. **Vierordt:** Arch. f. physiol. Heilk., xi. 1852, pp. 327, 854. **Welcker:** Henle u. Pfeufer's Ztschr. f. rat. Med., Dritte Reihe, xx. H. 1 and 2, p. 257; *also*, Arch. d. Ver. f. gemeinsch. Arb. z. Förd. d. wissensch. Heilk., Götting., 1854, p. 161; *also*, Vrtljschr. f. d. prakt. Heilk., Prag., xliv. 1854, p. 11; *also*, Arch. f. mik. Anat. viii. 1872, p. 472.

Estimation of the Richness of the Individual Corpuscles in Hæmoglobin.

361. In judging of the colour of the blood in anæmia, it was the custom, in earlier times, to regard the hæmoglobin in the corpuscles as of stable quantity. On this hypothesis, all that was thought to be necessary in order to arrive at the true value of the corpuscles as bearers of oxygen was to count their number.

Johann Duncan's researches, however (No. 12, lv. Ab. 2, 1867, p. 516), threw a new light on the subject, by showing that in cases of chlorosis, the amount of hæmoglobin, or colouring matter,

may be diminished out of proportion to the reduction in the number of corpuscles. In most instances of anæmic blood, the number of hæmocytes is reduced as well as the colour, but cases have been recorded of great anæmia in which the number was normal or even augmented.

Malassez and Hayem, besides confirming Duncan's observations, have gone much more fully into the matter.

Hayem (No. 218, p. 55) clearly points out that any method of estimating the amount of **aglobulia** or deficiency in hæmoglobin, must necessarily be faulty if founded upon the numeration of the corpuscles alone. In order to arrive at a true statement of the relative richness of each blood corpuscle in hæmoglobin, other factors must be taken into account. The quantity of hæmoglobin per cubic millimètre must first be found by the most approved colorimetric method. Hayem indicates this by the letter "R." Let us suppose that, in the blood under examination, it corresponds to a colour equivalent to blood containing 2,000,000 corpuscles per cubic millimètre. Let us further suppose that the blood in question contains 4,000,000 corpuscles per cubic millimètre. Then the richness of each corpuscle is $\frac{2}{4}$ or $\frac{1}{2}$; that is to say, each corpuscle contains only half the quantity of Hb which should be present in health. Hayem represents this by the letter "G."

It sometimes happens, however, that in anæmia the corpuscles are very irregular in size, some of them below, others above the average. It is therefore necessary to bear this in mind in making any statement as to the corpuscular richness of a particular blood.

In forming a correct estimate of the individual corpuscular value in hæmoglobin, Hayem holds that it is essential to attend to the following points:—

(1) The *richness* (R) of the blood in hæmoglobin expressed in terms of that of sound blood.

(2) The *alterations in size and shape* of the corpuscles.

(3) The *absolute number* of corpuscles (N), as calculated by counting.

(4) The *globular value* of the individual corpuscles (G).

THE EFFECTS OF HÆMORRHAGE UPON THE COMPOSITION OF THE BLOOD.

362. **The liquid part**, of course, suffers temporary diminution in quantity. When an *excess of liquid* is poured into the blood it is rapidly *excreted by the kidneys*, and continues to be so until the natural bulk of the blood is reached. The same tendency towards an equilibrium is noticed *when blood is withdrawn*. Liquid is soon abstracted from the tissues in quantity sufficient to compensate for the loss.

Bizzozero and Salvioli show that it is not absorbed immediately, but that from six to forty-eight hours' time is required before the former bulk is regained.

The blood, consequently, after **repeated hæmorrhages**, becomes *more and more watery*, and the number of corpuscles, as shown in the accompanying table of the results of experiments made by Vierordt,[1] progressively diminishes both relatively and absolutely.

Amount of blood extracted expressed as a fraction of the body weight.[2]	Proportion of red corpuscles expressed in hundredths of the normal proportion.
0	100
$\frac{1}{100}$	89
$\frac{1}{47}$	81
$\frac{1}{30}$	75
$\frac{1}{18}$	69
$\frac{1}{17}$	52
	Death of the animal.

Hæmoglobin.—With the loss in blood, of course, where the quantity is considerable, the number of coloured blood corpuscles diminishes, and with them, also, the amount of hæmoglobin.

Bizzozero and Salvioli (No. 225, xii. p. 611) showed that, after loss of blood by venesection, the quantity of hæmoglobin diminishes, from a few hours up to two days. A rise in the quantity takes place subsequent to this. This decrease comes on after depletions which do not reach 2 per cent of the body weight. For every per cent loss of blood as compared with the body weight, there is a diminution of 11·14 per cent of the original hæmoglobin, a result which they account for by the absorption of plasmatic fluid from the tissues.

363. **Hæmocytes.**—It has been found that after *a single large abstraction* of blood from an animal, the morphological characters of the coloured corpuscles alter. Many of them become irregular in shape—**poikilocytes** as they are called—and numerous very small corpuscles or **microcytes** make their appearance. Cells of diameter intermediate between these microcytes and an ordinary coloured corpuscle are also found, specially in Man. **Giant blood corpuscles** or **megalocytes,** running up to 14 μ in diameter are not usual as a result of a single large hæmorrhage, but *when the losses of blood are repeated* at comparatively short intervals, so as to set up a truly anæmic disease, they begin to show themselves.

The leucocytes are *increased in number*, both relatively and absolutely (Henle, Remak, Moleschott, Vierordt, Bauer, C. Weber, Osler). This is due to several causes, among the most important being, firstly, that the coloured corpuscles escape more readily from the blood-vessels, and hence leave a relatively large number of leucocytes behind; secondly, that the large quantity of lymph which rushes in to replace the bulk of the blood carries with it many new leucocytes; and,

[1] Quoted by Immermann, No. 206, vol. xvi. p. 328.

[2] Unfortunately the intervals between the various abstractions of blood are not mentioned, and the author cannot at present lay his hands upon the original paper.

thirdly, that the wound made in extracting the blood, if suppurating, is a fertile source of the leucocytosis. Malassez, indeed, goes so far as to say, that if there be no wound and no suppuration, there is no increase in the colourless corpuscles, but this is doubtful.

The hæmatoblasts or blood plates at first suffer a *decrease in number* along with the hæmocytes, until a minimum point is reached. There next follows a period of *increase* before the coloured corpuscles have begun to show evidence of replacement. A third period ensues in which the number of hæmatoblasts becomes *normal*, while the coloured corpuscles show signs of having been regenerated.

Fibrin.—The experiments of Brücke, Nasse, Sigmund-Mayer, and Jurgensen on the dog, and, more lately, those of Hayem, have shown that a single large loss of blood causes the fibrin to *diminish* in quantity, whereas repeated small hæmorrhages cause it to *increase*.

Venesection in Disease.

364. It is generally stated by physiologists, at the present day, that, as a quantity of blood equivalent to something like 3 per cent of the body weight may be abstracted without materially influencing the blood-pressure, phlebotomy must be useless in lowering the blood-pressure in disease.

Conclusions based upon observations made on the system in health are, to say the least of it, dangerous, if applied to it under disease, unqualified by further experiment. It may be true that loss of blood, even up to a large amount, has little effect upon the pressure in health, but this fact cannot be used as an argument against phlebotomy as a remedial agent in acute inflammations. Where the vessels of an important organ, such as the lung, are engorged with blood, and where the small arteries throughout the body are in a state of spasmodic rigidity, next to nothing is known with exactitude of its physiological effects. A very great deal, however, is known empirically to the physician, or rather was known to the older physicians, of its action under such circumstances. The older physicians were familiar with the experience that as the blood flowed from the arm in a patient moribund from acute croupous pneumonia, the inspirations became deeper and the general respiration easier; the rigid pulse gave way to one soft and yielding; and that in a large proportion of cases which otherwise would certainly have proved fatal, progress towards recovery was uninterrupted from the hour in which the blood was withdrawn.[1] Such facts were realised in the everyday practice of the past generation of physicians, but unfortunately those of the present day incline to look askance on the procedure. The fashion of the time stigmatises it as unwarrantable, and it is only a few individuals who have the courage to question the verdict. It is pleasing to notice, however, the reaction

[1] The author is able to confirm these assertions from considerable personal experience.

that is now setting in in favour of this sovereign remedy; and there is good reason to believe, that the younger members of the profession may live to see the time when stimulants to enable a heart to drive blood into a lung whose *viæ* are obstructed by excess of blood, carbonate of ammonia to tickle the patient's air passages, and beef steak to keep up his strength, will not be considered sheet-anchors to hold fast by in the treatment of a patient suffering from acute pneumonia.[1]

Not that these remarks are intended to lend countenance to bleeding as a remedy in all forms of inflammation of the lung. Every physician recognises that there are pneumonias and pneumonias. It is the employment of venesection in the wrong kind of pneumonia which has brought discredit upon the practice. The majority of

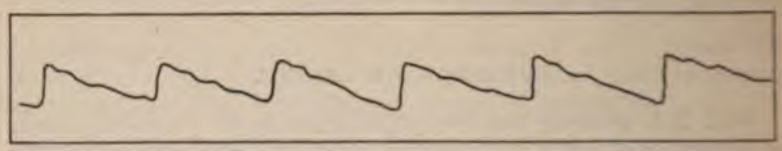

FIG. 179.—TRACING OF RADIAL PULSE BEFORE A HÆMORRHAGE.

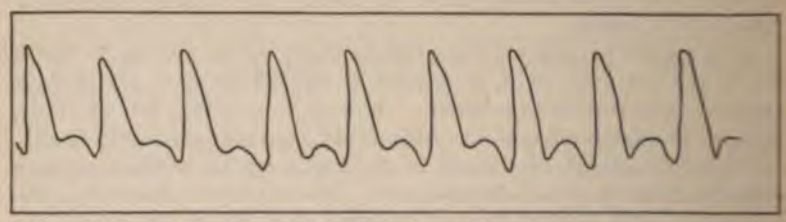

FIG. 180.—TRACING OF RADIAL PULSE AFTER A HÆMORRHAGE.

croupous pneumonias undergo spontaneous resolution, but it is in the cases of difficulty that the skill of the physician ought to show itself, and it is just in these very cases that modern treatment is so lamentably feeble.

365. **Guides as to the Quantity to be Withdrawn, etc.**—On an average, the loss of a pound of blood will induce syncope in a fully-grown person; and a quantity equal to half of the whole blood in the body (four to six pounds), when lost, must be regarded as sufficient to cause death (Wagner). Women bear losses of blood better than men, and the abstraction of a relatively small quantity may prove fatal in a child. Old people and those previously debilitated bear venesection badly, and the more rapidly it is withdrawn the more potent are the immediate physiological effects.

366. **Circumstances under which Venesection is calcu-**

[1] See admirable remarks by Broadbent (No. 6, 1887, i. p. 712) on this subject.

lated to afford Relief.—These may be summed up in one expression—*high arterial tension.* Venesection should not be resorted to in all cases where high arterial tension is present, but where high arterial tension is endangering life, as in acute pneumonia, blood-letting is one of the readiest means of reducing it.

Literature on Effects of Venesection on the Blood.—**Bauer:** Zeitschr. f. Biol., viii. 1872, p. 567. **Broadbent:** Lancet, 1883, i. pp. 4, 54. **Burman:** Lancet, 1883, ii. p. 856. **Corson:** Phila. Med. and Surg. Rep., xlvi. 1882, p. 365. **Dunn:** Boston Med. and Surg. Journ., May 11th 1882, p. 437. **Fenwick** (in Heart Disease): Lancet, 1882, ii. p. 179. **Genzmer:** Centralbl. f. d. med. Wissensch., xx. 1882, p. 225. **Johnson:** Med. Press and Circ., March 26th 1879, p. 242. **Maas:** Deut. Zeitschr. f. Chir., xvii. **Maragliano:** Centralbl. f. d. med. Wissensch., xviii. 1880, p. 867. **M. Hall:** On Morbid Effects of Loss of Blood. **Phillippart:** Bull. d. l'acad. de méd. de Belgique, No. 1, 1883, p. 128. **Sanquirico:** Arch. per le Scienze Mediche, vi. 1882, No. 10. **Silva:** Rivista Clinica di Bologna, No. 12, 1883. **Traube** (in Fevers): Gesam. Beiträge, ii. 1871, p. 212. **Vierordt:** Arch. f. physiol. Heilk., xiii. 1854, p. 259. **Volkmann:** Hæmodynamik. **Woltersom:** see Donders Physiol. d. Menschen, i. p. 170. **Wylie:** Glasg. Med. Journ., April 1883, p. 256.

Effects of certain Physiological Conditions upon the Composition of the Blood.

367. **Digestion.**—During the time that digestion is going on, it has been found (Hayem, Dupérié, Cadet) that the number of coloured corpuscles sinks while that of the leucocytes rises (leucocytosis of digestion). The number of hæmatoblasts also increases.

According to Dupérié (No. 212; No. 49, 1879, i. p. 40) the ingestion of food causes a diminution of the coloured corpuscles and an increase in the colourless. Long fasts have the effect of increasing the coloured, and the longer the interval between meals, the greater the number. A rich **nitrogenous** or a **mixed diet** has no effect upon their number, but a **vegetable** or a **milk diet** causes an increase in the leucocytes.

Other observers do not seem to have arrived at like results. Much, no doubt, depends upon the accuracy of the method of counting employed, and the precautions taken to avoid error due to extraneous circumstances.

Cutler and Bradford's (No. 179, i. 1878-9, p. 427) series of observations, made according to Malassez' method, before and after dinner, would tend to show that there was a very notable *increase* (in one case considerably more than one-third of the whole) *of the coloured*, and a by no means inconsiderable *decrease of the colourless* after food. Halla (No. 141, 1883, p. 198) has not observed a physiological increase, as Virchow had supposed there was, of the leucocytes after taking food, neither in health nor in disease.

368. **Over-Nourishment.**—Where an excess of proteids is supplied to the blood, it is evidently capable of taking them into its substance up to a certain limit. The condition is known as **hyperalbuminosis** or **plethora hyperalbuminosa.** It is questionable

whether they can be retained in the blood for long. Egg albumin, when transfused, is rapidly thrown off by the kidneys. The normal quantity of serum-albumin in human serum is from 70 to 90 parts per 1000, and it is probable that if this quantity is overstepped, grave mischief results to the blood as a circulating liquid. Where there has been excessive loss of liquid from the blood, as in cholera, or from copious diarrhœa, or where there is grave alteration in the number and quality of its corpuscular elements, as in certain cases of anæmia and in leucocythæmia, a spurious hyperalbuminosis may result.

Inanition.—The effects are, at first, chiefly manifested in the condition of the plasma, whose albumin sinks until it may reach something like 60 to 50 parts per 1000, or even less. The condition is known as **hypalbuminosis.** The *gross bulk* of the blood does not appear to suffer much as compared with other parts of the body, the albumin being compensated for by the absorption of water and salts. It is universally agreed that the *coloured corpuscles* do not decrease in number until the very latest stages, indeed, the recent researches of Hayem, Dupérié, Cadet, and Reyne seem to show that, as a rule, they are increased. By some observers, the *leucocytes* have been found to be diminished, by others, to be normal. The *hæmoglobin* begins to decrease only after a week's fasting. Even the *albumin* does not decrease so rapidly as might be expected.

A condition of hypalbuminosis is frequently occasioned by the escape of albumin through the kidneys in Bright's disease.

Literature on Effects of Inanition on the Blood.—**Bidder and Schmidt:** Die Verdauungssäfte u. d. Stoffwechsel, 1852. **Chossat:** Recherches expérimentales sur l'inanition, 1843. **Heidenhain:** Disquisitiones, 1857. **Panum:** Archiv. f. path. Anat., xxix. 1864, p. 241. **Pettenkofer and Voit:** Zeitschr. f. Biol., 1869, p. 369; Sitzungsb. d. k. bayerischen Akad. d. Wissenschaft., Nov. 10, 1866. **Valentin:** Repertorium, iii. **Voit:** Ztschr. f. Biol., ii. 1866, p. 307; *Ibid.*, viii. pp. 297-388.

369. **The term Plethora** seems to be a very indefinite one. The popular meaning of it is, that "full-blooded" persons possess an unusually large quantity of blood in their systems. An increase of the quantity of blood beyond a particular limit is proved to be an impossibility. When the quantity rises beyond a certain standard the bulk is reduced by excretion of its liquid. It is probable that the full-blooded appearance of plethoric individuals is due either to impeded circulation or to their possessing a luxuriant store of hæmoglobin.

Plethora apocoptica (Wagner, 211, p. 545) is the name given to that variety of plethora which results from driving the blood back from a limb into the general circulation as by the application of an Esmarch bandage. It causes no rise in the blood-pressure.

Polycythæmia rubra is the designation applied to a condition where the coloured blood corpuscles are in excess. An excess of blood corpuscles above the usual number (5,000,000 per cu. mm.) is rare. The supposed excess of coloured corpuscles is probably, in reality, an excess of hæmoglobin.

370. **A decreased supply of water** to the blood brings about a concentration of its solids. The quantity of *albumin* and *salts*, and, later on, that of the *urea* is increased. The term **hydræmia** is applied to a watery state of the blood, in a somewhat loose sense. *Temporary hydræmia* may be the result of increased consumption of liquid, or of liquid transfused directly into the circulation. The excessive liquid is, however, very soon thrown off by the kidneys.

As the bulk of the blood tends, as before explained, to maintain an equilibrium in bulk by absorption of water from the tissues, etc., hydræmia may also be the result of loss in the blood solids. A hydræmic state of the blood usually interferes with the functions of most organs, particularly with those of the stomach and intestine, and, through them, with the general nourishment of the body.

371. **Menstruation.**—The quantity of blood lost at each menstrual flux being from 100 to 200 grm., the effect on the general mass of blood must be considerable. Contrary to what might be expected, the *number* of coloured corpuscles increases (Hayem, Cadet, and Dupérié), but there is a sinking in the quantity of *hæmoglobin*. At the same time, there is a large accession to the number of *small coloured blood corpuscles* or *microcytes* (Cadet, No. 213, and Dupérié, No. 212). The *hæmatoblasts* or *blood plates* are also increased in number.

372. **Pregnancy.**—According to Quinquad (No. 214, p. 239) and others, the *hæmoglobin* is always below the normal in pregnancy, in some cases more than in others, corresponding to the various accidents that may be encountered during utero-gestation. Immediately after accouchement, for two or three days, the quantity of Hb becomes still lower.

Not only the hæmoglobin, but the *coloured corpuscles* have been found by numerous observers to be below the normal number, particularly during the later months of utero-gestation.

373. **Sex.**—The most recent researches on the subject of sex in relation to the composition of the blood point to there being a *poverty of coloured corpuscles in the female* as compared with the male. Taking the average number per cu. mm. at 5,000,000 for the male, Hayem finds that the average female blood gives only 4,500,000. The quantity of *hæmoglobin* is also *less* in the female than in the male (Leichtenstern). The blood of particularly stout persons usually contains a *small amount* of hæmoglobin, and it reaches its lowest limits in *chlorosis*, and *pernicious anæmia*.

Age.—The blood of the *new born* is characterised by the *greater variations in the size* of its corpuscles as compared with those of the adult (from three to ten μ), most of them being of large size. Their *number* appears to vary more than in adolescence (between 4,500,000 and 6,900,000 per cu. mm.—Hayem). The number of *leucocytes* is also very high for some days after birth, and the *hæmatoblasts* or *blood plates*, although less numerous at time of birth, gain the normal average in about nine days (Cadet, *loc. cit.*).

The blood of the child of a few years is *less rich in corpuscles* than that of the adult, and it is also poorer in *hæmoglobin*.

In *adolescence* it gains its *maximum* of *hæmoglobin*, the *small* and *large corpuscles* are *less numerous*, and the *number of corpuscles remains pretty steadfast* at the figures previously quoted.

In *old age* the *number* of corpuscles falls again to 4,956,000 (Cadet and Dupèrié) that of the *leucocytes* to 6000, and that of the *hæmatoblasts* to 255,000, per cu. mm.

Leichtenstern (No. 215, 1887, xxiv.; also No. 49, 1877, i. p. 236), employing Vierordt's method of estimation, finds, in accordance with the previous conclusions of Denis and Pogiale, and Panum, that the quantity of *hæmoglobin* in newly-born children is very large—30 per cent greater than in the adult. It rapidly sinks during the first few weeks of extra-uterine life, and reaches a minimum at from two to five years of age. From this date it again rises and reaches a second but smaller maximum at from thirty to thirty-five years. Towards the fiftieth year and beyond this it sinks, and, in old age, probably rises.

Pathological States of the System which Influence the Coagulation of the Blood.

374. The recent doctrine on the subject of the coagulation of the blood in health has been briefly stated under "Inflammation" (Sect. 145). The pathological factors which tend to alter its coagulability are :—

(1) *ACUTE PHLEGMASIÆ.*

375. When blood is withdrawn from a vein in Man, it usually begins to coagulate in from two and a half to three minutes, and in the course of ten to twelve hours a firm, tough, and contracted clot has formed, from which the serum has, in part, been squeezed out. The upper stratum of the clot, if formed in a tall vessel, is slightly more transparent and paler red than the parts lower down. The surface may actually be yellow coloured. The slower the coagulation, the more of this clear stratum forms on the surface. In the horse, whose blood coagulates slowly, the upper half of a mass of blood may present this pale yellowish-pink layer, composed of fibrin and serum almost free from blood corpuscles.

The more fibrin the blood contains, the slower it coagulates, and the more of this yellow layer is consequently seen upon the surface.

In *acute inflammations or phlegmasiæ* such as *croupous pneumonia, pleurisy, pericarditis*, in *acute rheumatism*, and in several other diseases, the amount of fibrin is increased, and the blood tends to coagulate slowly. A dense buff-coloured layer of fibrin consequently forms on the surface, called by the older physicians the **crusta phlogistica**.

The large proportion of fibrin in the coagulum in such cases tends to cause the clot to contract to an unusually great extent, and pulls the surface inwards. A cup-like depression is thus produced upon it.

Hence such a clot was said, in olden times, to be both *buffed* and *cupped*. The other characters of inflammatory blood, as Hunter (No. 128, i. p. 235) describes them are, that it "has an increased disposition to separate into its component parts, the red globules become less uniformly diffused, and their attraction to one another becomes stronger, so that the blood when out of the vessels soon becomes cloudy or muddy and dusky in its colour, and when spread over any surface, it appears mottled, the red blood attracting itself and forming spots of red."

The *red corpuscles*, when examined microscopically, instead of forming islands of *rouleaux* surrounded on all sides by plasma, rather incline to accumulate in *compact heaps* which are in contact at their circumferences. The *colourless corpuscles* are more numerous, and the fibrin threads are easily recognised on account of their number and density. In acute inflammations terminating suddenly in resolution, the fibrin can be seen to become daily less abundant.

The separation of the blood into the crusta and deep red coloured part is usually said to be owing to the corpuscles being heavier than the plasma. It has been held that as the corpuscles tend to run together into masses, these sink more readily than do the corpuscles in healthy blood,[1] and that this, taken along with the fact of the slow coagulability of the fibrin, and probably an alteration in the specific gravity of the plasma, account for the precipitation of the corpuscles towards the bottom of the vessel in which the blood may have been received.

Gulliver (No. 19, lxiv. p. 360, 1845) brought out some curious facts bearing upon this matter, and not by any means supporting the theories just referred to. He made out that the corpuscles sink at least twice as fast in the entire mass of blood, during the formation of the buffy coat, as in the serum alone. The falling of the corpuscles is rather retarded than hastened by a thinning, and hastened by a thickening of the liquor sanguinis. The corpuscles of horse's blood sink quicker in human serum of sp. gr. 1032 than in their own serum of sp. gr. 1028.

It may be urged, of course, that these experiments were made in a very rough manner (merely watching the sinking of the corpuscles in a tall vessel). Their incongruity with other known facts shows the utter futility, as before pointed out (Sect. 344), of drawing any conclusions as to specific gravity from dead blood, more especially when it is in large mass. Blood which is shed is blood no more, and it is very probable that, instead of the coloured blood corpuscles being so much heavier than the plasma, as is generally supposed, their specific gravities are almost identical in *living* blood as it circulates in health. (See Chap. xiii.).

The amount of fibrin which separates from normal blood is about 2·5 parts in 1000 (Gamgee). **In disease** it may amount to

[1] The corpuscles fall much faster after the first two or three minutes than before, probably from their becoming aggregated into heaps.

as much as 10 parts in 1000 (hyperinosis) or it may sink considerably below the normal (hypinosis). It is much increased in all grave acute inflammatory diseases, and slightly so in chlorosis, pregnancy, trivial inflammatory affections, and in certain cases of scorbutus (Gamgee).

(2) *HÆMOPHILIA OR PURPURA HÆMORRHAGICA.*

376. It has been suggested that the cause of this disease, in which there is a tendency to incontrollable hæmorrhage from various parts of the body, is a diminished proportion of fibrin in the blood. Such is not found to be the case. In most of the diatheses in which there is this tendency to bleed (gout, scorbutus, etc.) the fibrin is said to be sometimes rather increased than decreased.

(3) *PRESENCE OF BILE ACIDS.*

377. Icteric blood, after death at least, has frequently little tendency to coagulate. Bearing upon this, Nauck (No. 217, 1886), as Samson-Himmelstjerna had previously demonstrated, finds that bile-acids added in the proportion of 2 per cent to unfiltered, and in that of 1 per cent of filtered plasma, entirely prevent coagulation.

(4) *PEPTONÆMIA AND TRYPTONÆMIA.*

378. Peptone (Schmidt-Mülheim) and Tryptone (Albertoni) when injected into the blood, have been found to suspend coagulation (No. 247, 1880, p. 50). Fano (No. 49, 1882, i. p. 131) states that peptone does not interfere with coagulation when mixed with blood outside the body, but only when it is injected into the blood-vessels of a living animal. Schmidt-Mülheim found that the peptone disappeared rapidly from the blood; and Fano believes that the greater part of the peptone absorbed from the alimentary canal, or introduced into the circulation by artificial injection, is converted into albumin (globulin). The elements which bring this about are the coloured blood corpuscles. Fano (No. 51, Phys. Ab. 1881, p. 277) gives 0·3 grm. peptone mixed with a 0·5 per cent salt solution for each kilo weight of the animal, in animals up to 10 kilos, as being best suited to obtain a satisfactory result. The quantity of the peptone dissolved in the salt solution was usually 10 per cent.

The blood remains fluid for days if removed immediately after the injection, and the procedure is more effectual if the peptone is injected rapidly. In three hours afterwards, it coagulates as usual. If a second injection of peptone be made after this, it has no effect, even if the dose be larger. After twenty-four hours, however, the peptone acts as usual. He believes that a substance is generated in the blood which hinders coagulation, and which in course of time becomes

destroyed. If peptone blood be mixed with normal in equal quantities, its coagulability is destroyed.

With *tryptone*, and by that he understands pancreatic peptone, he has not been so successful, although, physically, it seemed to be identical with ordinary *peptone*. As a rule, peptone has little or no effect upon the blood of rabbits.

(5) *MORBID STATES OF THE BLOOD-VESSELS.*

379. Wherever there is any roughness of the lining membranes of the heart or blood-vessels, there is a tendency for the blood to coagulate upon the roughened part (see Sect. 208). **Acute endocarditis, acute arteriitis** or **phlebitis**, or a **varicose state of the veins** of a part, particularly predispose to the local precipitation of blood-clot.

(6) *IMPEDED RESPIRATION.*

380. In conditions where the natural interchange of gases in the lung has been interfered with to such an extent as to have brought about a fatal result, as in death by hanging, the blood remains more or less uncoagulated.

The **inhalation of oxygen,** on the contrary, renders coagulation after death more complete.

(7) *SUDDEN SHOCK.*

381. In cases where death occurs suddenly, as from lightning, a fall from a height, a blow on the solar plexus, or from sun-stroke, the blood is said to remain liquid after death, or to coagulate only very softly. Very much the same statement was made by John Hunter, but some of the causes alleged by him to bring about this result require reinvestigation.

(8) *HYPINOTIC DISEASES.*

382. In those diseases in which the blood contains a small proportion of fibrin, such as scorbutus and typhus fever, the coagulation after death is feeble.

Literature on Coagulability of Blood in Disease.—**Addison:** Lond. Med. Gaz., i. 1841, pp. 477, 689. **Davy:** Phil. Trans. Lond., cxii. 1822, p. 271. **Flint:** Buffalo M. J., xii. 1856, p. 65. **Gulliver:** Edin. M. and S. J., lxiv. 1845, p. 360. **Hayem:** Soc. méd. d. hôp., 1881. **Hayne:** Med. Jahrb., Wien, xlviii. 1844, p. 146. **Jones (T. W.):** Report on the Changes of the Blood in Inflammation, and on the nature of the Healing Process. **Naunyn:** Arch. f. exper. path. u. Pharmakol., i. 1873, p. i. **Richardson:** Fibrinous Elements of the Blood in Relation to Disease, 1851; *also*, The Cause of the Coagulation of the Blood (Astley Cooper prize essay), 1858; *also*, On Fibrinous Deposition in the Heart, 1859. **Scudamore:** Essay on the Blood, etc., 1824. **Taylor:** Lond. Med. Physiol. Journ., xi. 1831, p. 187. **Vierordt:** Arch. d. Heilk., xix. 1878, p. 193. **Virchow:** Archiv. f. path. Anat., i. 1847, p. 547; *Ibid.*, ii. 1848, p. 587; *Ibid.*, v. 1852, p. 43. **Wunderlich:** Arch. f. physiol. Heilk., i. 1842, p. 459.

EXTRANEOUS CIRCUMSTANCES AFFECTING COAGULATION.

383. **Rapidity of Stream.**—It is generally admitted that blood drawn gradually, coagulates more rapidly than when it flows in a full stream (Richardson, No. 220, p. 27).

384. **Shape of Vessel.**—Coagulation takes place slowly when the blood is allowed to run into a tall vessel. Richardson (*loc. cit.*), influenced by the theory that free ammonia is the agent which prevents the blood from coagulating spontaneously, accounted for it by the tall vessel hindering the ammonia from escaping.

385. **Agitation.**—Moderate agitation in the open air is said to favour it, while agitation in a closed vessel retards it (Richardson, *loc. cit.*, p. 28).

386. **Presence of Oil.**—Freund (No. 229, 1886, p. 296) states that, if blood be allowed to escape from a severed carotid under oil, or into a vessel smeared with vaseline, it does not coagulate at the ordinary temperature of a sitting-room within twenty-four hours after being shed, not even when stirred with a clean glass rod. If it be prevented from drying, and be protected from dust, it will remain liquid for days, and affords a means of obtaining a complete separation of the blood corpuscles from the supernatant plasma.

If a glass tube coated with vaseline be placed in the carotid, a clot is not precipitated upon it.

Haycraft (No. 189, July 1887) made a parallel set of experiments, and arrived at very much the same conclusions.

The above, however, constitute no new experience. Magendie (No. 59, 1838-9, i. p. 635) found, on mixing freshly-drawn blood with oil, that the coagulum which formed was particularly soft. Babington (referred to by Richardson from oral communication) discovered, when he immersed the head of a cock under oil, and in this position cut the head off and allowed the blood to settle to the bottom of the vessel, that coagulation was very much retarded. Richardson (*loc. cit.*, p. 209) made a number of experiments on the same subject, finding that coagulation was retarded by covering the blood with oil, and that the coagulum, when formed, was particularly soft.

387. **Salt Solution.**—If fish bladders, or parchment tubes swollen in physiological salt solution be filled with blood from a cannula coated with vaseline, and be afterwards hung up in salt solution, coagulation does not occur within twenty-four hours, nor is there any exudation of the colouring matter. The blood remains as in a living vessel (Freund, *loc. cit.*).

388. **Leech Secretion.**—Haycraft (No. 149, 1884, No. ccxxxi.) discovered that the medicinal leech secretes from its mouth a fluid which prevents coagulation, he believes, by destroying the blood ferment.

389. **Presence of Free Ammonia.**—Free ammonia prevents coagulation. Richardson was led to believe (*loc. cit.*) that during life

sufficient free ammonia was present to retain the blood in a fluid state. The theory is, however, not generally entertained at the present day.

390. **Temperature.**—A low temperature materially retards coagulation. If the blood be frozen within a vein and subsequently thawed, it will still be found to be fluid, and will coagulate in a few minutes afterwards (Hewson, No. 230, p. 17). Heat, on the other hand, as demonstrated by Hewson (*loc. cit.*, p. 4), tends to hasten coagulation.

391. **Other Circumstances.**—The admixture of various salts has the power of retarding or entirely preventing coagulation, and a similar effect is noticed when egg albumin, syrup, glycerine, mucilage, or water, in quantity, is added (Hewson, Gulliver, Richardson).

Fate of Transfused Blood.

392. Some interesting points bearing upon the pathology of the blood are opened up by the subject of **transfusion.** Does the removal of the fibrin unfit the blood for the needs of the organism, and how soon is the fibrin restored? What is the history of blood transfused from one animal to another of the same kind? What becomes of transfused blood taken from an animal of a different kind?

Dumas and Prevost (No. 222, 1821, T. 17; Ann. de chimie, 1821, T. 18, p. 294) and J. Müller (No. 223, i. p. 124) seem to have been the first to make out that defibrinated blood could be transfused with impunity. Magendie (No. 224, T. iv.) found, when blood is withdrawn from a dog, defibrinated, and again injected, that there followed hæmorrhagic œdema of the lungs, together with hæmorrhages into, and capillary injection of, the mucous membrane of the intestine, and he supposed that one of the functions of the fibrin must be to favour the passage of blood through the capillaries.

Panum, however (No. 13, xxvii. 1863, pp. 240 and 433), after many experiments, was unable to confirm this. He found that the deprivation of the blood of its fibrin has no marked effect so long as the animal is of the same species, and explains Magendie's results by the collateral circumstances of the experiment. Fibrin is reproduced in its normal amount in at least forty-eight hours (Panum) after being abstracted in as great quantity as possible.

Lower (No. 174) proved that an animal could live when its blood was entirely substituted by that of another animal *of the same species.* He bled a dog of medium size from the jugular vein until it became collapsed and convulsed. He then allowed the blood from the crural artery of a second dog of large size to run into the opened vein until, he says, it became evident that the first dog was distended with blood. He stopped the transfusion at this point, and again allowed the blood to escape from the vein. This was repeated until the small dog had received the blood of two such large dogs, so that there was good reason to believe that there had been a complete substitution of the foreign blood for that properly belonging to the animal. When the subject of the experiment was released, it

sprang actively from the table, and continued to run about in higher spirits than it had been before the operation. The experiment did not seem to have deleteriously affected its well-being in the slightest degree. A commission appointed by the Philosophical Society of London to inquire into the matter, repeated the experiment with like results.

The animals, moreover, continued permanently in good condition, showing that the corpuscles are not destroyed, but that, when transfused from the vessels of one animal into those of another of the same species, they continue to circulate and to supply the wants of the system.

Panum (*loc. cit.*, p. 453) has repeated these experiments, finding, in order that the experiment may be successful, that the blood must be filtered through fine linen. He states that the entire blood of an animal, or at least down to 3 per mille, can be replaced by the defibrinated blood of another animal without material injury.

There seems, in bygone times, to have been considerable diversity of opinion as to what comes of the blood corpuscles when taken from an animal of a *different* kind. Marfels and Moleschott (No. 225, 1856, i. p. 51) recognised the blood corpuscles of the sheep in the circulation of the frog months after they had been transfused, and Brown Séquard (No. 226, i. p. 173) detected blood corpuscles of the dog a month after they had been transfused into the vessels of geese and fowls. Magendie (No. 59, 1838-39, i. p. 889), however, although he could inject 4 centilitres of dog's blood into the circulation of a bird with impunity, found that *the corpuscles became destroyed or modified in such a manner that, in course of time, none but normal corpuscles were discoverable.*

Magendie's results are now pretty generally accepted. The presence or absence of foreign corpuscles after their transfusion, no doubt, depends upon the time which has elapsed. One thing seems certain, namely, *that they are not regenerated.*

Between *animals closely related*, blood can evidently be interchanged with impunity, such as the blood of the calf for that of the lamb (Rosa), and horse's blood for that of the ass (Edwards), but in the case of Man it has been found that *it is safe to transfuse only from one individual to another.*

TRANSFUSION INTO THE PERITONEUM.

393. From the fact that liquids are so rapidly absorbed from the serous cavities, it has been suggested that blood might be transfused into the vessels through the peritoneum instead of into the vessels directly. It has also been supposed that blood effused into a tissue might be absorbed back into the circulation.

Historical.—According to Hunter (No. 5, xxi. 1887, p. 139), Karst (No. 43, 1873, p. 587) seems to have originally drawn attention to this peritoneal absorption

of blood, but, of late years, it has been made the subject of searching inquiry by Bizzozero and Golgi, Quincke, Hunter, and others.

Hunter (*loc. cit.*) shows that in animals, if sufficient precautions are taken, considerable quantities of blood can be injected into the peritoneal cavity with impunity.

Ponfick (No. 43, 1879, p. 589) suggested its use in persons suffering from **anæmia**, and put it into practice in several cases. Others have since then also employed it. The results are not encouraging, for although in certain instances it seems to have done good, yet in others severe and fatal peritonitis resulted.

Fate of the Corpuscles.—An interesting question comes to be, *whether the corpuscles get back into the circulation uninjured and fit for circulation purposes.* Bizzozero and Golgi (No. 50, xvii. 1879, p. 917) found that, in rabbits, a large number of the blood corpuscles injected into the peritoneum made their way back into the blood-vessels. In twenty minutes after injection there was a distinct increase in the number in the vessels, and the maximum was reached on the first or second day. The richness in hæmoglobin was estimated, with the result that its quantity corresponded to that of the blood injected. The highest increase, however, did not amount to more than 57 per cent of that originally present in the circulating blood. The increase lasts more than a week, and in one animal they found a sensible increase after twenty-seven days. The augmentation takes place both when the animal is unaltered and when it is rendered artificially anæmic previous to the experiment.

The excretion of the excess of corpuscles from the blood, according to Quincke (No. 140, xxxiii. 1883, p. 22), causes a deposition of iron albuminate in the bone marrow, in the spleen, and in the leucocytes of the liver capillaries, exceptionally also in the gland cells of the liver and kidney. Jaundice did not follow repeated subcutaneous injections of blood.

Hunter (*loc. cit.*) very properly particularises the durability of the corpuscles within the vessels as being the matter of real importance. The presence merely of free hæmoglobin in the blood is absolutely useless as an aid in the economy of the system. It is soon all removed, mainly through the agency of the liver. It is different when coloured corpuscles are actually introduced into the circulation. While they remain, they perform functions similar to those already present, and afterwards perish in a like manner.

SYSTEMATIC EXAMINATION OF THE BLOOD.

394. The methods of preparing the blood for ordinary histological examination have already been detailed (Sect. 145). It only remains now to say that the anatomical examination of any sample of blood in order to be complete should comprise (1) that of its histological characters; (2) the determination of the power of coloration (Sect. 349); and (3) the numeration of its corpuscles (Sect. 357).

CHAPTER XXXI

THE BLOOD—*Continued*

Sources of the Blood Corpuscles.

395. The organs engaged in the *manufacture*, if the term may be used in such a sense, of the blood corpuscles during the periods of intra-uterine or extra-uterine existence, do not appear to be exactly alike. The **liver** is evidently one of the chief blood corpuscle forming organs during the former, while in the latter this function seems to be completely annulled. As the known pathology of the blood is almost exclusively confined to extra-uterine life, the remarks on its formation presently to be offered, will be limited to this phase of existence.

396. **Rapidity of Reproduction.**—The rapidity with which the blood corpuscles are repaired in Man seems to be considerably influenced by collateral circumstances. A good deal evidently depends upon the amount lost. In the case of *passive hæmorrhages*, such as hæmoptysis or metrorrhagia, it has been calculated by Hayem, Hünerfauth, and Kermisson that a loss of from 340 to 350 grammes (10 to 12 oz. av.) is regenerated in from ten to fifteen days. A similar quantity lost traumatically or during a surgical operation is recovered more slowly. Kermisson (No. 205) explains this apparent anomaly by the disturbance caused to the whole system by shock.

Repeated hæmorrhages in an otherwise healthy individual, have a more deleterious effect upon the regenerating powers of the blood-forming organs than a single large hæmorrhage.

a. Sources of the Leucocytes.

397. The most important possible sources are the following :—

(1) From leucocytes pre-existing in the blood.

(2) From the lymph glands.

(3) From the spleen and bone marrow.

(1) *FROM LEUCOCYTES PRE-EXISTING IN THE BLOOD.*

398. If the presence of multiple nuclei were to be regarded as evidence of cell division, there would be good reason for believing that, as the colourless corpuscles circulate, they are also engaged in regenerating themselves. It seems improbable, however, that the double or tripartite nucleus frequently seen in them is an expression of this (Virchow, Löwit). In mammals it is usually regarded as a sign of degeneration.

It has been asserted by Klein (No. 50, 1870, p. 17), however, that in the triton's blood, a true division of the colourless corpuscles is to be noticed, and the fact that a karyomitotic network is frequently present within them, would point to the possibility at least, of its taking place.

Löwit (No. 12, lxxxviii. Ab. III. H. i.-v. 1884, Jahrg. 1883, p. 356) found evidence of indirect division in the **coloured corpuscles**, but never in the colourless, either in circulating blood, or in blood-forming organs. He regards regenerative division of any kind in **leucocytes** circulating in the blood as, at all times rare. Flemming (No. 86), Peremeschko (No. 14, vi. 1880), and Arnold (No. 13, xcvii. 1884, p. 107), however, admit of its occurrence.

Bizzozero (No. 208, xxxvi. 1885, p. 365) states that indirect division goes on actively within the leucocytes in leucocythæmia.

It would therefore seem, that although certainly the division of a leucocyte in circulating human blood may at times be met with, yet that the number which are regenerated by this means must be comparatively small.

(2) *FROM THE LYMPH GLANDS.*

399. Authors are pretty well agreed, that, if these are not the only source of the leucocytes present in the blood, they must at least be one of the most fertile. The blood of the right side of the heart is considerably richer in leucocytes than that of the left, most probably from the lymph corpuscles poured into it from the various lymph channels.

(3) *FROM THE SPLEEN AND BONE MARROW.*

400. The **spleen** has long been held to be an organ concerned in the formation of leucocytes, more especially since it was shown by Bennett and Virchow to be increased in size in **Leucocythæmia**, a disease in which the colourless corpuscles are in great excess in the blood. The enlargement of the spleen is chiefly due to an accumulation of these cells within it, and hence the association of its function with that of the preparation of the leucocytes in health followed as a natural consequence. Schultz (No. 210, pt. ii. p. 497, quoted by Virchow), called the spleen "a mesenterial gland of the stomach," and Virchow, in considering the lymph glands as a possible source of the

colourless cells in Leucocythæmia, gives support to this idea. He would thus account for the simultaneous implication of the lymph-glands and spleen in that disease.

The blood of the splenic vein is elsewhere referred to (Sect. 410) as containing more coloured blood corpuscles than that of the **splenic artery**. There has been, until lately, an almost universal concensus of opinion that it also contains more leucocytes.

Hirt, experimenting upon the calf, found the proportion of colourless to coloured to be as 1 : 70 in the splenic vein, while it did not amount to more than 1 : 2000 in the artery. Funke,[1] made out the proportion in the splenic vein of the horse to be as 1 : 3 or even 1 : 2 ; while Vierordt,[1] alleged that in Man it was 1 : 4·9 in the vein; and Frey[1] as 1 : 102.

Gibson (No. 5, xx. 1886, p. 353), on numerating the corpuscles by modern methods, found the proportion in the splenic vein of a dog to be as 1 : 701·1, in the artery as 1 : 781·2.

Tarchanoff and Swaen (No. 4, ii. 1875, p. 324), also employing modern methods of numeration, have placed the number of leucocytes contained in the vein even below that of the splenic artery. The following table represents the results of four observations made by them upon the blood of the splenic artery and vein in the dog.

(*a*) Blood of the splenic artery	8,200	wh. corp.	per cu. mm.
,, ,, ,, vein	7,600	,,	,,
(*b*) Blood of a short splenic artery	10,100	,,	,,
,, ,, ,, veinule	4,300	,,	,,
(*c*) Blood of a splenic artery	8,600	,,	,,
,, ,, ,, veinule	5,800	,,	,,
(*d*) Blood of the splenic artery	5,800	,,	,,
,, a splenic veinule	7,900	,,	,,

From these results, they say, it follows "*that the blood of the splenic vein, far from containing an enormous quantity of white globules, in reality contains fewer than that of the artery.*"

It would therefore seem, that a number of the colourless cells which enter the spleen by the artery are either destroyed or are retained within it. Dilatation of the spleen, such as that which follows section of its nerves, causes the number retained to be still greater, it may be, by opening up the cavernous structure of the organ, and rendering the liability of the leucocytes becoming entangled in it greater.

The figures quoted from Funke, Vierordt, and Frey are manifestly far too high, owing to faulty methods of examination, while Gibson's figures come much nearer the truth. Observations made after death are worthless, and hence those made on Man must be put out of account. It seems, moreover, to be likely that the number of leucocytes may vary with the general condition of the animal at the time of observation.

There is no doubt that the matter is open to fallacy, and that further experiments, carefully conducted, and often repeated, are

[1] Quoted by Tarchanoff and Swaen, No. 4, ii. 1875, p. 324.

necessary to arrive at accurate conclusions. The number of leucocytes to be found, in the human spleen at least, under what might be considered analogous conditions, almost suggests that they are stored up in its substance at times, to be given off to the system as required.

If there be a paucity of colourless corpuscles returning from the spleen, the theory which regards it as a colourless corpuscle forming organ would seem to have no foundation; indeed it is more just to conclude that at least some of the colourless corpuscles entering it are destroyed, mostly by becoming converted into coloured blood corpuscles.

In support of the latter view it is urged that **excision of the spleen** causes a leucocytosis (Zesas, Winogradoff, Tauber, and Gibson), evidently by abolishing its blood transforming functions. In course of time, this leucocytosis disappears, and coexistently, the **mesenteric lymph glands**, and in certain cases the **bone marrow,** become vascular and crowded with half transformed blood corpuscles, obviously pointing to the existence of a compensatory function in these structures.

The **red bone marrow** is also held by some to be a source in health of the leucocytes, while others as regularly deny any action of this kind possessed by it. Large numbers of cells, identical with leucocytes, are certainly found within it (see Sect. 412), but whether these are to be regarded as having sprung directly from it, or merely as having been sifted out of the blood circulating through its porous structure, is open to question.

It seems to be certain, however, that having accumulated here, from whatever source, they subserve a most important purpose by becoming transformed into coloured blood corpuscles.

GENERAL CONCLUSIONS IN REGARD TO THE ORIGIN OF THE COLOURLESS CORPUSCLES.

401. It seems, therefore, pretty clear (1) that the main source of the blood leucocytes is the lymph glands.

(2) The spleen and bone marrow are probably the seat of development of some of them, but not of the majority.

(*b*) Sources of the Hæmocytes.

402. The alleged sources of these will be considered in the following order:—

(1) From pre-existing corpuscles of the same kind in the blood itself. (2) From blood leucocytes. (3) From the hæmatoblasts or blood plates. (4) From the endothelium lining the walls of the minute vessels.

(1) *FROM PRE-EXISTING CORPUSCLES OF THE SAME KIND IN THE BLOOD ITSELF.*

403. Seeing that the coloured blood corpuscles of mammals, with the exception of the camel and llama, do not possess a nucleus, it is hard, at first sight, to conceive of their regeneration by division. From the fact, however, that these mammals have nucleated corpuscles, and also seeing that the embryo mammalian blood corpuscles are nucleated, there is the possibility that those of Man, under certain conditions, might develop a nucleus.

This actually happens in disease. Klebs (No. 13, xxxviii. 1867, p. 190) appears to have discovered them in a case of *leucocythæmia*, but of late they have been found in many other morbid states such as *chronic secondary anæmia* (Litten and Orth, No. 43, Jahrg. xiv. 1877, p. 743), *pernicious anæmia* (Cohnheim, No. 13, lxviii. 1876, p. 291; Ehrlich, No. 43, Jahrg. xviii. 1881, p. 43, and many others), *septicæmia*, *typhoid*, *phthisis*, *carcinoma*, *tabes*, *pleurisy*, *pneumonia*, etc. In fact, in most diseases accompanied by *malnutrition*, they appear to be present with considerable regularity.

The significance of the nucleus, however, must not be misinterpreted. It cannot be regarded in the light of a step towards the propagation of new corpuscles from the old by division, but rather as evidence of incomplete sanguification, whereby the nucleus of the cells (leucocytes or hæmatoblasts), out of which the coloured discs are naturally evolved, has not been thoroughly transformed into their homogeneous substance. A certain number of cells has thus been allowed to enter the blood in an immature condition.

Arnold (No. 13, xcvii. 1884, p. 107) finds that they are sometimes **polynucleated.** Ehrlich distinguishes three different varieties according to their size—**normoblasts, megaloblasts,** and **mikroblasts** or **poikiloblasts.** The last of these are seldom met with, while the normoblasts occur in simple anæmia and in leucocythæmia, the megaloblasts in pernicious anæmia.

Hayem (No. 4, iii. 1873, p. 369) likens these nucleated coloured blood corpuscles to the blood-generating cells (hæmatoblasts) of bone marrow described by Neumann. He says that they are never in great number, and he believes that, when they do become transformed into fully developed blood discs, it is not by a mere coloration and shrinking of their substance, but by their giving rise to his hæmatoblasts or blood plates which, in their turn, develop into fully formed blood corpuscles.

Indirect Division.—In the lower vertebrates, however, division of the nucleus of the coloured corpuscles by *karyomitosis* has, of late, been frequently observed. Bizzozero and Torre (No. 13, xcv. 1884, p. 1) have studied it in gold-fish, in reptiles, and in amphibia. In all the fully grown vertebrates examined, they state that, in certain organs at least, there is evidence of indirect division of the nucleus of the coloured blood corpuscles, while in the gold-fish they probably divide directly. In mammals, birds, reptiles, and anoura, the division takes place in the bone marrow; in the urodela, in the spleen; and in fish in the spleen and lymph-gland-like substance of the kidney. In triton, the division can be seen proceeding under the eye within from fifteen to twenty minutes. Aly (No. 203; and No. 49, 1884, p. 59) supports

Bizzozero's statements, and says that, in triton cristatus and rana esculenta and temporaria, karyomitosis can be seen proceeding in the living state without the aid of staining. Indirect division has also been studied by Eberth (No. 11, iii. 1885, p. 1). He finds that there are large and small coloured blood corpuscles in the blood of the freshly caught triton. In the spleen there are three varieties of these small corpuscles. The one is yellow stained and devoid of a nucleus, the other unpigmented and with a large round nucleus, while yet others are seen which are somewhat elongated, and which have yellow protoplasm. In the last of these, he has noticed nuclear plexuses, on the warm stage, undergoing mitotic transformation, and ending in division.

(2) *FROM BLOOD LEUCOCYTES.*

404. The notion that the coloured corpuscles are developed out of the colourless has long been entertained by physiologists of proved capacity.

Wharton Jones (No. 65, 1846, p. 63 *et seq.*) described how, in the fish and frog, the red blood corpuscles arise from the colourless by their granular contents becoming homogeneous and their substance stained; while in mammals and in Man they were to be regarded as the product of the transformed nucleus.

Rindfleisch (No. 201) adopted very much the same view regarding their development in mammals and in Man, and held that the nucleus was extruded from the cell body.

Klebs (No. 13, xxxviii. 1867, p. 190), although agreeing with the foregoing observers so far, in regarding the colourless as the progenitors of the coloured, yet differed from them as to the manner in which it is accomplished. He thought that, in Man at least, he saw the periphery of the cell, not the nucleus, become pigmented. **Kölliker's view** (No. 235, p. 533) of their development in the adult, practically coincides with this. The whole subject, he remarks, is problematical, but it is most likely that the coloured discs are developed out of the chyle corpuscles by losing their nuclei and becoming flattened, while hæmatine forms in their interior.[1]

Erb (No. 13, xxxiv. 1865, p. 138) states that, in the case of the fowl from which blood has been withdrawn and in which regeneration is proceeding, coloured corpuscles in great number are always to be met with, which contain in their interior various small and large granules and a nucleus exactly resembling those of the leucocytes. He thinks that these must be regarded as the immediate transitional forms between the colourless and the coloured elements. He also saw these transitional forms in the rat, calf, and cat, but in the full-grown ox, horse, sheep, and pig, they were absent. When however, animals, in whose blood during health they were not to be discovered, are starved, transitional forms begin to develop in abundance.

v. Recklinghausen (No. 14, ii. 1866, p. 137) describes coloured corpuscles as developing in the blood of the frog from leucocytes, when the blood was withdrawn from the body and kept in a moist chamber. The leucocytes throw out processes which become disunited from the parent cell and transformed into coloured corpuscles.

Feuerstack (No. 112, iv. 1883, p. 345) found forms transitional between the colourless and coloured in the fish, after several blood lettings. They are spherical,

[1] Gibson's views (*op. cit.*) are quite in harmony with Kölliker's description. They are more fully detailed in Section 416.

coloured cells, with unusually large nucleus (Neumann's hæmatoblasts), and are simply the colourless corpuscles whose cell body has become hyaline and coloured. The cell body gradually increases in circumference and assumes a flattened aspect, while the nucleus is reduced in size.

Loewit (No. 12, xcii. Ab. iii. 1885; and No. 22, x. 1885, p. 136) recognises two distinct varieties of colourless corpuscle, regarded in the light of their future life history. The one set he names **leucoblasts** (λευκός, white), and the other **erythroblasts** (ἐρυθρός, red). The leucoblasts possess amœboid movements, they absorb cinnabar, are often more granular than the erythroblasts, and, when about to become destroyed, show evidence of cleavage. The erythroblasts are hæmoglobin free, show no amœboid movements, and do not absorb cinnabar particles. Their nuclei contain a chromatophylous threadwork, and they proliferate by karyomitosis. The chief distinctive point between the two is, that whereas the leucoblasts remain as such in the blood, the erythroblasts are transformed into coloured blood corpuscles. The erythroblasts take their origin in the lymph glands, and are poured in large quantity, along with the lymph stream, into the circulating blood. Their transformation into ordinary coloured blood corpuscles takes place in the bone marrow.

Specious as these numerous observations may appear to be, it is only just to add that many recent workers of the highest authority have asserted that the colourless and coloured corpuscles have no genetic relationship. Virchow (No. 13, v. 1853, p. 43) long ago upheld the doctrine that the colourless and coloured corpuscles are entirely separate entities, and that they are not developmentally connected.

In later times, Neumann, Hayem, Bizzozero, and Osler, have reasserted these views, holding that a transformation of the one into the other can no longer be entertained.

Hayem, Bizzozero, and Osler, all seem to have arrived at very much the same conclusion, namely, that the colourless corpuscles constitute a distinct element of the blood, and that they are isolated in their origin, life history, and functions from the coloured. As Osler remarks (No. 199, xxix. 1886, p. 377 *et seq.*), their functions seem to be multifarious. "They are utilised in the repair of wounds and in the reproduction of tissues; they act as scavengers or phagocytes in removing dead parts, in inclosing injurious particles in their interior and rendering them inert—a standing army ready to resist the invasion of parasitical micro-organisms."

(3) *FROM HÆMATOBLASTS OR BLOOD PLATES.*

405. Hayem (No. 4, v. and vi. 1878, p. 692) described the hæmatoblasts or blood plates as subserving a twofold purpose, namely, that of *renovating the blood by becoming converted into coloured blood corpuscles, and of playing an active part in coagulation.* With the latter of these functions we are not immediately concerned (see Sect. 145).

When he made this announcement, the matter of course was very carefully gone into by numerous collateral workers, more especially by Bizzozero and his followers. As a result of their researches, they were unable to confirm what Hayem had stated as to their being a source

of coloured blood-corpuscle genesis, and, of late years, discredit has rather fallen upon Hayem's view.

Hayem traced their connection with coloured blood corpuscles in the following manner:—Within the blood, there are always to be seen a certain number of abortive coloured corpuscles or microcytes. These, he holds, are hæmatoblasts (blood plates) in process of becoming transformed into hæmocytes.

That these microcytes are derived from blood plates has been strenuously opposed by the most recent workers on the subject.

It is only fair to add, however, that there are other circumstances which favour Hayem's view of the evolution of coloured blood corpuscles out of his hæmatoblasts, namely, that, after hæmorrhage, they appear in great numbers before the reparation of the coloured corpuscles has commenced; and as the number of the latter increases, that of the hæmatoblasts decreases.

Affanassiew (No. 91, xxxv. 1884, p. 215; No. 208, xxxv. 1884, p. 217; No. 50, li. 1884) endorses almost all that Hayem has written on this subject, but further adds that they undergo transformation into coloured blood corpuscles within the marrow of bones. His venesection experiments on dogs also show that the blood plates increase vastly in number when the animal becomes anæmic, and when the repair of the blood is proceeding. Under such circumstances, numbers of deformed, or *bizarre*, coloured corpuscles (poikilocytes) show themselves in the blood. He grants, however, that there may be other means by which the coloured corpuscles are regenerated.

Crise hématique.—Hayem finds that in *critical* diseases there is a profound alteration in the blood just at the time when the crisis is approaching. It consists in a sudden *rise in the number of blood plates*, which he designates by the above name. It begins when the temperature commences to sink, and reaches its height usually on the day when the temperature becomes normal. The ordinary proportion of blood plates to red corpuscles is as 1 : 20. In acute fevers the proportion sinks as low as 1 : 18 or 1 : 12, but, at the time of the crisis, it again rises as high as 1 : 7, and he asserts that, during convalescence, they become converted into blood discs.

(4) *FROM THE ENDOTHELIUM LINING THE WALLS OF THE BLOOD-VESSELS.*

406. Although there is little doubt that in the embryo the corpuscles are actually formed out of the walls of the minute rudimentary blood-vessels, yet such a mode of origin in the adult has never been conclusively proved. Division of the endothelium in the wall of the minute capillaries has already been referred to (Sect. 167) as being supposed by Wharton Jones to account for many of the colourless cells which appear in and around the small vessels in inflammation.

(c)—Sources of the Hæmatoblasts.

407. What little is known on this subject is referred to in Section 418.

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The Organs which Transform the Colourless Corpuscles into the Coloured.

408. We have now seen that the colourless corpuscles, in all likelihood, become transformed into the coloured, but we have not traced

how this is accomplished. The two organs, if we may designate the latter as such, in which the conversion of the one into the other chiefly occurs, are generally held to be **the spleen** and the **red marrow of bones.** The **lymph glands** and the **thyroid** have also been considered to possess such properties, and it now remains to examine in how far such assumptions are justifiable.

(1) *THE SPLEEN.*

409. The spleen has always been regarded, more or less, as an organ concerned in the fabrication of the coloured blood corpuscles as well as of the leucocytes, the usual theory being that coloured blood corpuscles are both destroyed and regenerated within it. These ideas first gained a footing chiefly from the following facts: (1) Cells containing coloured blood corpuscles in their interior are occasionally met with in its substance. The corpuscles are supposed to have been intussuscepted, and to be in process of becoming dissolved by the enveloping cell protoplasm; (2) cells which are evidently rudimentary coloured blood corpuscles are found within it, especially in cases where the repair of the blood from loss is actively proceeding.

410. **Method of Investigating the Blood-forming Functions of the Organ.**—The mere histological examination of the healthy spleen affords very little conclusive information of its blood corpuscle forming powers. The facts to be derived from it constitute only one link in the chain of evidence. The further methods that have been employed of late consist (*a*) in the accurate numeration of the coloured corpuscles and of the quantity of hæmoglobin contained in the splenic artery and vein; (*b*) in the study of the organ after venesection; and (*c*) in the study of the blood after splenotomy. It will be well to follow these three methods in tracing the evidence of the blood corpuscle transforming powers of the organ.

(*a*) **By Enumeration of Corpuscles and Estimation of Hæmoglobin.**—Malassez along with Picard (No. 40, lxxxii. 1876, p. 855) established, by actually counting the blood corpuscles per cubic millimètre, that the blood of the splenic vein contained more coloured corpuscles than that of the splenic artery. Many of the hæmocytes coming from the spleen by the vein also correspond to what are generally recognised as "immature forms."

On carefully enumerating the corpuscles in the splenic vein and artery, Gibson (*loc. cit.*, p. 353) found, three days after a dog had been rendered artificially anæmic by a single abstraction of 2·6 per cent of the body weight of blood, that the proportion was as follows:—

Splenic Vein.

Hæmocytes 6,310,000; leucocytes 9000 per cubic mm. Relative number of leucocytes to hæmocytes 1 : 701·1.

Splenic Artery.

Hæmocytes 6,250,000; leucocytes 8000. Relative number of leucocytes to hæmocytes, 1 : 781·2. This would therefore show, as his other experiments bear out, that the splenic vein contains both more coloured and more colourless corpuscles than the splenic artery.

Tarchanoff and Swaen (see Sect. 400) admit that the coloured are more numerous in the vein, but that the colourless are relatively fewer than in the artery.

Of course, it must always be borne in mind, that in order to produce a recognisable increase in the number of either corpuscle in every small portion of blood leaving the spleen, the addition must have been very considerable, and hence fallacious results might easily be obtained. The whole subject of the enumeration of blood corpuscles is so liable to lead into error, that too much care cannot be taken in drawing conclusions from it.

Bizzozero further supports the assumed blood corpuscle forming property of the organ, by the fact that in many animals the quantity of **hæmoglobin** found in the blood of the splenic vein in health is greater than that in the splenic artery. After *extirpation of the organ* it diminishes throughout the general circulation, but rises again, sometimes rapidly, at other times more slowly, probably from the lymph glands assuming splenic functions.

(*b*) **By Venesection.**—The effect of venesection upon the blood corpuscle transforming properties of the spleen seems to vary a good deal according to the animal employed, and hence such a method of experiment may lead to miscalculation of its powers in this respect.

Neumann appears to have inferred, from experiments performed upon the *rabbit*, an animal in which it is comparatively inert, that the spleen was not a blood corpuscle transforming organ. In *dogs* it appears to be much more active.

Bizzozero and Torre (No. 133, vol. iv. 1880, p. 388; No. 49, 1880, i. p. 33) saw nothing in their investigations to convince them that it has a blood corpuscle transforming function in *birds*, but rather concluded that the bone marrow is the organ concerned.

Aly (No. 203) and Eberth (No. 11, iii. 1885, p. 1) both agree that in the *water-newt* the spleen is the active coloured blood corpuscle transforming organ, while in the *frog* the bone marrow appears to take its place.

Korn's experiments (No. 50, xli. 1880) on *birds*, on the other hand, tend to prove that such a property does reside within the spleen even in birds, although perhaps in a minor degree, and point to the reciprocal relationship that appears to exist between the spleen and bone marrow as hæmopoietic viscera. When the spleen is removed in birds, the **bone marrow** of the hollow bones becomes intensely red from the richness of its blood in hæmoglobin and from the appearance of numerous embryonic blood corpuscles within it. These alterations are not confined exclusively to bones containing marrow. The hollow air-containing bones, in time, also become filled with red marrow and new blood-vessels.

Neumann[1] is stated to have found a similar reciprocal action of the bone marrow

[1] Referred to by Gowers, No. 209, v. 1879, p. 272.

in a *dog* from which the spleen had been removed ten months previously. There was great increase of the lymphoid cells and intermediate forms within it, as compared with the normal medulla of dogs, or with that a few days or weeks after removal of the spleen. Such, however, has not been the invariable experience of those who have performed this experiment. Mosler failed to discover anything of the kind.

Bizzozero and Salvioli (No. 133, iv. 2, 1880, p. 49; No. 50, xvii. 1879, p. 273; No. 49, 1880, i. p. 33) state that, in *dogs and guinea-pigs*, the number of nucleated, that is to say, of transitional coloured corpuscles to be found in the spleen, corresponds with the amount of blood withdrawn from the general circulation. When the experiment succeeded in calling forth its blood forming properties, they found it to be swollen, like bone marrow, of a characteristic rose red colour, and rich in nucleated blood corpuscles. The blood of the splenic vein contained very large, pale red, blood corpuscles, and in the systemic circulation nucleated forms were twice observed. There was also a large excess of colourless corpuscles. They therefore hold that the spleen must be intimately connected with the reparation of the coloured elements.

Gibson (*loc. cit.*, p. 350) showed that, three days after withdrawing 2·6 per cent of the body weight of blood from a dog, the spleen was unusually large, soft, succulent, and of a rose red colour. On examining it microscopically, there was found to be an increased number of transitional nucleated red corpuscles. Enormous numbers of such transitional blood corpuscles were also met with in the bone marrow, and a few in the lymph glands.

Feuerstack's experiments (No. 100, xxxviii. 1883, p. 136) seem to corroborate those of many other observers in the same line of research. After repeated venesections in animals, the number of colourless corpuscles in the spleen, or, at any rate, cells that he took for such, increases. Forms which are transitional between these and a coloured disc, next make their appearance by the pigmentation of the foregoing. These pigmented transitional cells gradually expand and become flattened, while the nucleus shrinks. From the fact that it thus becomes altered after venesection, and also seeing that it is reproduced when excised in the *eel*, he concludes that the spleen must subserve a very important purpose as a blood forming mechanism.

(*c*) **By Splenotomy.**—The experiments have either been of the nature of simple excisions, or have been combined with *removal of the thyroid* or with *venesection*.

Malassez (No. 204, xxvi. 1878; No. 49, 1878, i. p. 140) employed dogs as the subject of experiment, and found on accurately counting the coloured blood corpuscles before and after the operation of excision of the spleen that their number diminishes in the first few days from its removal. After one month, it becomes higher than normally. On carefully estimating the amount of hæmoglobin, he discovered that it falls at first, and again, in course of time, reaches the normal standard.

Winogradoff (No. 49, 1883, i. p. 250) has studied the effects of excision of the spleen in three dogs with the following results: The number of coloured corpuscles fell suddenly at first, and continued to do so gradually on to the 150th or 200th day, but subsequently rose. During the first year, the dimensions and form of the corpuscles were not much altered. Numbers of small corpuscles or *microcytes* showed themselves after this. The *hæmoglobin* decreased, and the *specific gravity* of the arterial blood was *in toto* less, but the serum alone showed little alteration. The *dry residue* did not differ from that of normal blood. The *lymph glands* had increased in size and weight. They were soft, succulent, and dark or light red in colour from an accumulation of coloured corpuscles in the meshes of the gland tissue. The same congested appearance was found in the marrow of bones, unless in those of the paws.

Tauber (No. 49, 1883, i. p. 250) excised the spleen and thyroid in fifteen different animals, sometimes simultaneously, at other times successively. Between the two organs, he finds, there is no reciprocal connection. The animals become anæmic, and the relative and absolute number of colourless blood corpuscles is increased, while the size and number of the coloured decreases.

In all experiments where the spleen is excised, the number of coloured blood corpuscles seems to sink at first, but in course of time the blood evidently begins to recuperate itself, and the number rises. Tauber supposes that the recovery is due to an enlargement of the lymphatic glands, and Zesas (No. 92, xxviii. 1883, p. 815) not only confirms, in rabbits, what Tauber states as to the condition of the glands in dogs, but seems to think that the thyroid also participates in this compensatory action. Gibson (No. 5, xx. 1886, p. 340), also using modern methods of numeration, found that in a *dog* in which he excised the spleen, the number of *coloured corpuscles* sank considerably during the first two months, and there was a relative and absolute increase in the number of *colourless*. The greatest decrease occurred two months after the operation. After reaching a minimum, the red corpuscles increased again in number, though not very regularly; and the relation of the white corpuscles to the red, gradually approached that which had existed previous to the removal of the organ. His other experiments on the dog support these results.

The spleen has also been successfully removed in **Man,** when diseased, but unfortunately, the records of the condition of the blood and other matters of interest have not always been kept with that accuracy which might be desired.

One of the cases of greatest value, from the care taken to record the facts, is that reported by Credé (No. 92, xxviii. 1882, p. 401), in which the spleen was excised in a man 44 years old for a cyst contained in it. As is the case after excision of the organ in the lower animals, the leucocytes underwent great increase, the climax being reached in about two months, when their number, as compared with the red, was found to be 1 to 3 or 4. There was also a large proportion of small blood corpuscles or microcytes, some of them nucleated. Curiously, as if supporting Zesas' conclusions, the thyroid showed a painful swelling, which, however, subsided as the blood resumed its normal condition. In course of time, the Man completely recovered, and the blood assumed its natural appearance. Credé concluded:

(1) That the spleen can be successfully removed from Man in adult life.

(2) Its removal calls forth a profound disturbance in the fabrication of the blood.

(3) This derangement is compensated for by the vicarious action of the thyroid gland and bone marrow.

(4) The spleen subserves the purpose in health of transforming the colourless corpuscles into coloured.

411. **Summary.**—The presumptive evidence in favour of the spleen being a blood corpuscle transforming organ, so far as one can judge from experiments upon the lower animals and from the effects of splenotomy upon the blood in Man, is therefore undeniable. It evidently subserves a most important function *as a hæmopoietic organ* in Man and in certain mammals. When it is removed, *a sudden loss in the number of coloured blood corpuscles, followed by an increase of the colourless, ensues.* This condition of the blood continues for several months, but is recovered from in course of time.

(2) *THE BONE MARROW.*

412. **Its Structure.**—Bone marrow is of three varieties—the *yellow*, the *red*, and the *gelatinous*. The first is that which is found in hollow bones, the second occurs in short flat bones, while the third is found here and there in hollow bones.

The yellow marrow is made up in great part of fat cells, between which runs, as in ordinary fat tissue, a quantity of nucleated fibrous stroma.

The red marrow is much more vascular, and does not contain so much fat as the yellow. It occupies all the cavities of the bones in the fœtus, but, in the adult, is confined to the cancellæ of short flat bones, such as the bodies of the vertebræ, those of the tarsus and carpus, and the ribs. It may thus seem to be widely distributed, and to be of comparatively small bulk. If, however, the whole of it were reckoned as a single mass, it would considerably exceed the volume of the spleen.

Within its substance are contained cells of different kinds. In the first place, there are numerous **nucleated and coloured cells** known as **Neumann's hæmatoblasts**. As a rule, they are about the size of a leucocyte, and the colour they possess is due to their containing hæmoglobin. There is good reason to believe that they are of the same nature as the young nucleated and coloured cells found in the spleen after hæmorrhage—that they represent, in fact, *the transitional stage* between the leucocytes and the coloured blood discs.

These immature blood corpuscles are found scattered throughout the *substance of the bone marrow*, but they are also said to have been seen within the *lymph vessels and veins*, evidently on their way to join the blood current.

The *circulation* within the marrow is peculiar. It has been asserted by Hoyer (No. 50, xvi. and xvii. 1869) that the arteries open into *cavernous spaces* without distinct walls, from which, again, capillaries spring to join the veins. There is some doubt as to whether this has been actually established, but if it were true, the resemblance to the cavernous structure of the spleen would point to an existing homology between bone marrow and that organ. It might also account for the ready absorption of newly developed blood corpuscles from the substance of bone marrow.

Besides the hæmatoblasts, numbers of **uncoloured marrow cells**, almost the size of a colourless corpuscle or smaller, are to be seen in fresh red marrow, along with numerous **ordinary coloured corpuscles**. The latter are the main cause of the red colour of the marrow. **Large cells containing coloured blood corpuscles** are also occasionally met with. **Colourless marrow cells with peculiarly homogeneous protoplasm, distinct border, and ill-defined nucleus,** are also referred to by Obrastzow (No. 50, xviii.

1880, p. 453); Malassez (No. 204, xlix. 1881, p. 689); and Osler (No. 6, i. 1886).

Giant cells or myelo-plaques, large and small, are also found within the adventitia of the vessels, and elsewhere, in red marrow. With these we are not much concerned at present, seeing that their function is chiefly that of bringing about ossification.

Side by side with nucleated cells possessing no intranuclear network, Arnold (No. 13, xcvii. 1884, p. 107) finds giant cells in which the network is abundant, and in many instances the chromatic substance is spread out, not in the form of threads, but somewhat diffusely. He describes indirect division both in the large and small marrow cells.

The gelatinous marrow is evidently more œdematous than the other two varieties, and contains a *mucin-like substance* dissolved in its liquid (Krause, No. 207, p. 70). The fat cells of the yellow marrow, and the hæmoglobin-stained cells of the red are both absent from it.

413. **Methods of Examining Marrow in Health and Disease.**—The marrow should be examined microscopically, both in the fresh state and after having been subjected to reagents. Neumann particularly dwells upon the importance of examining it when quite fresh and unaltered by hardening or staining solutions. A piece of it is simply withdrawn with as little injury as possible, and pressed out under a cover-slip. If it be desired to fix the elements, a piece of marrow may be pressed on a slide and be subsequently subjected to the action of perosmic acid vapour (Malassez). If it is intended to examine the *mitoma* of the nuclei, Arnold (No. 13, xcvii. 1884, p. 107) recommends methyl-green in 0·6 per cent solution of common salt. The solution is much improved by the addition of 0·25 per cent gold chloride. He shakes pieces of bone marrow with this until the elements of the marrow become dissociated.

Gibson (*loc. cit.*, p. 344) coincides with Neumann in the importance of examining it when fresh. He recommends teasing it out, and gently pressing down with the cover-glass. He uses an artificial serum as a suspending medium, composed of sodic sulphate of 1022 sp. gr. and a very small proportion of methyl-violet. The latter, he says, in addition to colouring, appears to have the most useful property of fixing the protoplasm of the cells.

414. **Neumann's Discoveries.**—The recognition of the bone marrow as a probable birthplace of the coloured blood corpuscles, dates back to the time when Neumann (No. 50, vi. 1868, p. 689; No. 126, x. 1869, pp. 68 and 220; *Ibid.*, xii. 1871, p. 187; *Ibid.*, xv. 1874, p. 441; No. 169, ix. 1874, p. 110; No. 14, xi. 1874, p. 169; *Ibid.*, xii. 1876, p. 793), in his various publications made the very important discovery that the red bone marrow in health, and especially in disease, contains within its substance a large number of the nucleated coloured corpuscles or hæmatoblasts just referred to. He stated, as the result of his inquiries, that he believed the coloured corpuscles of mammals

were nucleated when young, and that their chief source was the bone marrow.

He found that these **nucleated blood corpuscles** were present in all **red marrow**, the more abundantly the younger the individual. He saw them also in the **yellow marrow**, but much more scantily than in the red. So long as the nucleus remains, they are considerably larger than an average coloured blood corpuscle, but, with the disappearance of the nucleus, the whole cell shrinks.

Similar cells are found in the spleen, and a few may be seen in lymph glands (Löwit). Neumann, however, believed that the spleen, if concerned at all in blood corpuscle formation, was only of secondary importance, and that their chief source was in reality the bone marrow (No. 91, iii. 1881, p. 411).

415. **Origin of the Neumann's Hæmatoblasts.**—There may be said to be two views on this subject, the one, that they are simply blood leucocytes which have become entangled and transformed in the marrow; the other, that they are developed by division from those cells *resident* in the marrow itself.

Of course, great difficulties stand in the way either of proving or disproving the first view, but it seems probable that a good many of them owe their origin to this source.

Whatever the origin of the hæmatoblasts may be, there seems little doubt that within the bone marrow they are subject to most active proliferative changes. Division among the cells of the medulla is seen proceeding with such rapidity, that Rindfleisch (No. 14, xvii.) declares to there being, second to cartilage, no cells so well suited to study cell proliferation in as the hæmatoblasts of a middle sized guinea-pig.

Bizzozero, moreover (No. 50, viii. 1881), describes their division in the bone marrow of birds by means of *karyomitosis*. He finds cells of oval or round shape, with a nucleus in the stage of the "equatorial disc;" oval cells with "daughter asters" and "glomeruli," often united by fine striæ; similar cells with completely separated nuclei and constricted protoplasm; and lastly, cells whose nuclei show the reticulum of the "resting stage."

Bizzozero and Torre also find (No. 13, xcv. 1883, p. 1) that, in various classes of animals, there are special organs in which indirect division can be detected in the younger forms of blood corpuscle. Thus in mammals, birds, reptiles, and tailless amphibians, it is the *bone marrow;* in tailed amphibians, the *spleen;* and in fish, besides the spleen, the *lymphoid parenchyma*, which, in them, includes the *kidney*.

416. **Transformation of the Hæmatoblasts.**—The cells of bone marrow that we have to do with at present, in studying the evolution of the coloured blood corpuscles, are, as before described, ordinary *leucocytes, leucocytes with homogeneous protoplasm, nucleated cells about the size of a leucocyte and coloured with hæmoglobin, larger cells containing blood corpuscles, and fully developed blood discs.* It now remains to be seen what the relationship between these different forms may be.

To begin with the leucocytes, we have already seen what their

various sources are (Sect. 397). It has also been mentioned as probable that the coloured blood elements are simply these leucocytes in a more advanced stage of evolution.

Rindfleisch, as previously mentioned, described the transformation as being caused by the rejection of the nucleus from the cell body. The cell body then closes in and becomes flattened, and thereby constitutes a coloured blood corpuscle. Facts are against this account of the process, and it is not generally accepted.

A much more feasible statement is given by Arndt (No. 13, lxxxiii. 1881, p. 17), namely, that the nucleus becomes transformed, partially or completely, into hæmoglobin, and that the amount of this transformation determines whether the blood corpuscle will be nucleated or not.

In describing the structure of red bone marrow, it was mentioned that blood corpuscle holding cells are occasionally seen in it. It has

FIG. 181.—STAGES OF TRANSFORMATION OF LEUCOCYTES OF BONE MARROW INTO HÆMOCYTES (after Gibson).

(*a*) Hæmatoblasts as yet unstained with hæmoglobin; (*b*) the body of the cell coloured with hæmoglobin; (*c*) same, with, in addition, a shrinking of the nucleus; (*d*) a still further shrinking of the nucleus and relatively increased size of the pigmented cell-body; (*e*) the nucleus quite rudimentary, the whole cell diminished in size; (*f*) nucleus disappeared, a mere depression left—formation of a coloured blood-corpuscle. The impregnation with hæmoglobin is represented by the shading.

been asserted by Foa and Salvioli (No. 133, iv. 1879; No. 49, 1879, i. p. 41) that, in the embryo at least, the coloured blood corpuscles are developed from **polynucleated giant cells.** The **nuclei** are liberated from the cells and become blood discs. It is quite possible that the presence of these giant hæmatoblasts may have given rise to the opinion that blood corpuscle holding cells are a normal constituent of bone marrow. They are pretty common in *pernicious anæmia*, but here of course there is always the other view admissible, namely, that they are in process of intussuscepting blood corpuscles and destroying them.

Arnold (*loc. cit.*, p. 15) admits, that the method of development of blood corpuscles within giant cells and their subsequent escape from the latter by rupture is a feasible method, and that it is borne out by fact.

He describes still another method by which giant cells may give birth to coloured blood corpuscles in bone marrow. A giant mass of protoplasm, without nuclei, becomes coloured with hæmatin. It subsequently splits into many fragments, each fragment becoming a blood corpuscle. What are called *microcytes*, or very small fragmentary looking corpuscles, are sometimes met with in great abundance in anæmia. It is possible, if this method of blood corpuscle development can be entertained at all, that it might account for their presence.

Gibson (*loc. cit.*, pp. 345, 467), on the contrary, scouts the idea of the giant-cells being parents to a progeny of blood corpuscles, and traces their origin to nucleated colourless cells (leucocytes). The leucocyte at first is, of course, devoid of colouring matter, and has the appearance represented in Fig. 181 (*a*). The next stage consists in a coloration of the protoplasm around the nucleus in a narrow band (*b*). The cell becomes progressively smaller and flattened, and the nucleus shrinks, while the margin of coloured protoplasm increases in size (*c*). The nucleus, lastly, becomes a mere point or shadow in the cell substance, and ultimately disappears (*d*, *e*, *f*).

This is substantially the view entertained by Kölliker, and there seems every probability that it is correct.

417. **Conclusions.**—(1) There is very good reason to believe that the bone marrow in Man subserves the same purpose as the spleen, in transforming the leucocytes into coloured blood corpuscles.

(2) The manner in which this is accomplished is, that leucocytes become entangled in its cavernous tissue; they next begin to show a yellow colour from the deposition of hæmoglobin in the protoplasm round their nuclei; the nucleus shrinks and disappears; and contemporaneously, the cell becomes flattened and reduced in size, so as to constitute a blood disc.

(3) *THE LYMPH GLANDS AND THYROID.*

418. That the **lymph glands** have any direct coloured corpuscle forming capacity in extra-uterine existence seems as yet to be doubtful. As previously explained, they may become coloured blood corpuscle forming organs when the spleen is excised, but otherwise, do not seem directly to contribute to their mass. Gibson (*loc. cit.*, p. 456 *et seq.*) seems to think that they may have some power of transforming leucocytes even in health. He found that they did so after tying the thoracic duct in a dog so as to delay the transmission of the leucocytes onwards.

Although not directly engaged in throwing off coloured blood corpuscles, yet there seems good reason to believe that the lymph glands subserve a most fundamental purpose in hæmopoiesis by furnishing the colourless cells (erythroblasts), which the bone marrow, and most likely the spleen, subsequently convert into hæmocytes (see

Sect. 404), and hence may be regarded as of primary importance in maintaining a healthy state of the blood.

If, moreover, we accept Hayem's hypothesis that his hæmatoblasts or blood plates are the immediate predecessors of the coloured corpuscles, the lymph glands stand out with an equally important genetic significance. In the account he gives of the origin of these hæmatoblasts, he says (No. 204, xv. 1879), that they develop within the colourless cells of lymph, and that they are usually discharged into the lymph before the latter enters the blood. He found lymph cells containing from one to three hæmatoblasts, in the juice expressed from lymph glands. The hæmatoblasts within them are highly refractile, stain orange-red with eosin, and are discharged by the amœboid movements of the cells in which they are retained.

It should also be mentioned, that Foa and Salvioli have found large numbers of immature nucleated blood corpuscles (hæmatoblasts of Neumann) in the lymph glands of the fœtal calf, but not in extra-uterine existence.

The removal of the **thyroid** brings about a grave constitutional disturbance (cachexia strumipriva) which indirectly may react upon the quality of the blood; but its blood forming capacity, although such is vouched for by some workers on this subject, seems still unsettled in the affirmative. Gibson (No. 5, xx. 1886, p. 674), from experiments on dogs, and from a careful perusal of the literature of the subject, concludes that the "thyroid has, properly speaking, no blood forming function." Any blood forming capacity which experiments on animals may have pointed to its possessing, he explains by the presence within it of lymph-follicle tissue.

General Summary of Conclusions regarding the Origin of the Corpuscular Elements of the Blood.

419. 1. Taking all things into consideration, there cannot be much doubt that the great source of the coloured corpuscles is to be found in the colourless.

2. The transformation does not take place to any great extent, if at all, in the general circulation, but in special organs provided for the purpose.

3. There is no evidence to show that the coloured increase in mammals and in Man by segmentation. The coloured are rather to be looked upon as an ultimatum in the evolution of the particulate matter of the blood. Having reached this and subserved their purpose as bearers of the respiratory gases, they perish.

4. Hayem has adduced strong arguments to show that coloured corpuscles are evolved from his *hæmatoblasts* or *blood plates*, but further investigation is required to establish the truth of this assertion.

5. The leucocytes are in all probability derived at first hand from

the lymph glands. They may perhaps subsequently increase in number by cleavage.

6. They seem to be of two kinds—leucoblasts and erythroblasts.

7. The functions of the former are not accurately known, but the latter evidently become transformed into coloured corpuscles in the spleen, and within bone marrow.

8. It is possible that the spleen and bone marrow also create leucocytes. Their structure seems, however, more adapted for sifting the leucocytes out of the circulating blood, and for retarding their onward progress, so that they may become loaded with hæmoglobin and undergo the other changes necessary to convert them into blood discs.

9. The starting point, therefore, in the history of the coloured blood corpuscles is their origin in the lymph glands; the second phase of their existence is where they are set free in the blood circulation; the third where they are entangled in the spleen and bone marrow; and the last where they are liberated from these organs as blood discs impregnated with hæmoglobin.

10. Those colourless corpuscles which do not become transformed probably subserve many useful purposes, such as removing dead tissues, and protecting the body against the invasion of micro-organisms.

11. The blood plates appear also to be derived from the cells of the lymph glands.

CHAPTER XXXII

THE BLOOD—*Continued*

ANÆMIA

NOMENCLATURE

420. THE term literally means *bloodlessness* (α priv., and αἷμα, blood). At the present day, however, it is not employed in the sense of indicating a diminution in the total *quantity* of the blood, but rather as pointing to a deficiency in its *quality*. That of **oligæmia** (ὀλίγος, little or few) is occasionally used in a like sense; and where the defect is in the number of corpuscles, the condition is sometimes expressed by that of **oligocythæmia** (κύτος, a cell).

Simon (No. 231, p. 306) introduced the term **spanæmia** (σπάνιος poor) to indicate a poverty of the blood in solids, more especially in corpuscles and fibrin. Hayem uses that of **aglobulia** (aglobulie) to express a deficiency in hæmoglobin. Its exact significance has been explained in Section 361. By **hyperalbuminosis** and **hypalbuminosis** are meant respectively an unusual richness and scarcity of the albumins; and similarly the terms **hyperinosis** (ἶς, ἰνός, fibrin of the blood) and **hypinosis** relate to an excess or deficiency in fibrin.

GENERAL CHARACTERS OF THE BLOOD IN ANÆMIA.

421. **Dimensions of Corpuscles.**—As a general statement, it may be said, that with the exception of anæmia produced by a single large hæmorrhage, the dimensions of the coloured corpuscles will be found to be modified. In chronic anæmia, it is common to find an excess of small corpuscles or **microcytes**, a condition which is sometimes so evident that the term **microcythæmia** has been applied to it by Masius and Vanlair (No. 232, 1871).

One of the most remarkable cases of this disease is recorded by the above authors. It was that of a young girl who suffered from chronic jaundice with splenic swelling. The microcytes almost entirely took the place of the ordinary coloured corpuscles.

When present, they are usually from 2 to 5 μ in diameter, incline to be spherical, and are sometimes deeply coloured.

Eichorst's Corpuscles.—A special form of microcyte (see Fig. 182) has been described by Eichorst (No. 233, p. 123 *et seq.*) in the blood of those suffering from **pernicious anæmia.** It is perfectly round, from 3 to 3·5 μ in diameter, and the individuals never run into rouleaux as evaporation is proceeding. Their protoplasm is homogeneous, and they have a deep red colour. They are destitute of a nucleus and are peculiarly resistant to all reagents which affect the ordinary coloured corpuscles. So numerous are they, that he could sometimes count 1 for every 5 ordinary coloured discs. He regards them as being almost diagnostic of pernicious anæmia, although Grainger Stewart (No. 6, 1876, ii. p. 40), Lépine (No. 234, 1876, Nos. cxiv. cxv.), Rosenstein (No. 43, February 1877, No. ix.), and Stricker (No. 22, Jahrg. ii. 1877, p. 287), have not been able to confirm this.

At other times there is a preponderance of very large or **giant corpuscles** running from 10 up to 14 μ in diameter.

Gram (No. 11, ii. 1884, p. 47) states that the diameter of the coloured blood-corpuscles in cases of **jaundice** is increased without their absolute bulk being augmented. Osler (No. 199, xxix. 1886, p. 377 *et seq.*) thinks that "there may exist in the (icteric) serum some element—the product of destruction in the hæmoglobin—which may act upon the red cells and cause them to assume a more flattened form."

Blood corpuscle holding cells have been alleged to be present, but this must be of rare occurrence, otherwise their presence would have been oftener confirmed.

422. **Form of the Corpuscles.**—Alterations in shape are very frequent. Thus the coloured corpuscles may be more or less pointed, balloon, or tadpole shaped, or they may be irregular in outline, the small varieties being those in which the deformity is greatest. They go by the name of **poikilocytes.**

423. **Colour and Number.**—Where the anæmia is at all advanced, the blood has a pale red watery appearance, with sometimes a tinge of yellow in it. The colour of the corpuscles in some forms is below that of health. Their number may not be absolutely diminished, and yet the anæmia be very evident, owing to the loss in hæmoglobin.

DEGREES OF ANÆMIA.

424. Various attempts have been made to classify anæmias according to the amount of aglobulia or deficiency in hæmoglobin which may be present.

Halla (No. 141, 1883, p. 198) recognises three possibilities: (1) the number of coloured blood corpuscles sinks lower than the so-called "richesse globulaire" (Hayem, see Sect. 361); (2) the colour sinks parallel with that of the coloured blood corpuscles, and still the latter retain their normal proportion of colouring matter; (3) the colour sinks along with the number.

425. According to the amount of aglobulia or deficiency in hæmoglobin, Hayem classifies anæmias in four categories :—

(1) *Slight aglobulia.*—There is some difficulty in saying when a particular blood is worthy of being called anæmic or aglobulic. It may, however, be generally classified as pathological when its richness (R) in hæmoglobin (see Sect. 361) is expressed by a value inferior to that of blood containing 4,000,000 healthy corpuscles per cu. mm. In this first degree of aglobulia the richness of the blood (R) in hæmoglobin ranges between an equivalent of 4,000,000 and 3,000,000. The globular richness of the individual corpuscles (G) may, however, vary according as the corpuscles are altered in number or not. In the present case it may sink to 0·90 or to 0·70 (1 representing the globular value of a corpuscle in health), while in a normal individual it seldom falls below 0·90.

(2) *Medium Aglobulia.*—This is characterised by a greater falling off in the hæmoglobin. When expressed in terms of healthy corpuscles, the blood sinks in colouring power to a value represented by 3,000,000 to 2,000,000 per cu. mm. The number of corpuscles, however, may be very large, owing to there being an excessive proportion of small and deformed corpuscles present. Many of these microcytes may be poorly coloured. There may on the other hand be many giant corpuscles present, but these being also weak in colouring matter, the total result of the calculation need not necessarily be interfered with, as might at first be expected. In estimating the value of the total result, the degree of colour of those abnormal corpuscles should of course always be borne in mind.

The absolute number of corpuscles in certain cases may even be above that of normal blood, but usually ranges between 5,500,000 and 3,000,000 ; and very often at the time when the patient is recovering the number may absolutely fall. The value of the individual corpuscles in hæmoglobin may sink to 0·30, that is to say, the blood, taken as a whole, is more than three times weaker in colouring matter than it should be in health. This, however, is considered a minimum. The corpuscular value ranges as a rule between 0·30 and 0·80.

(3) *Intense Aglobulia.*—As before, the corpuscles vary in dimensions, but the average size approaches that of the normal, sometimes above, sometimes below it. The proportion of small globules is not so great as before. Large and giant cells are more characteristic, although not invariably so.

The degree of globular richness (R), compared with that of sound blood, descends to an equivalent of 2,000,000 to 800,000. The number of corpuscles ranges between 2,800,000 and 1,000,000. The globular value (G) of the individual corpuscles, seeing that their number and richness in hæmoglobin (R) are reduced simultaneously, is higher than before. It varies between 0·40 and 1.

(4) *Extreme or Pernicious Aglobulia.*—It comprises those cases where the disease usually proves fatal. The impoverishment in coloured

corpuscles is often complicated by other alterations, particularly by leucocythæmia; but in certain exceptional cases the aglobulia appears to be primitive (essential, spontaneous), and constitutes the only anatomical lesion. It is accompanied, as in the preceding, by grave alteration in the size of certain of the coloured corpuscles, but the average approaches that of health. The richness in hæmoglobin (R) varies between an equivalent of 800,000 and 450,000 of healthy blood; the number of corpuscles is extremely small, relatively less than that which represents its richness in hæmoglobin; and the globular value of the individual corpuscles approaches the normal.

VARIETIES OF ANÆMIA.

426. The varieties of anæmia, considered from an etiological basis of classification, are so numerous that it would be out of place to refer to them all at present. A few of the most typical forms may, however, be specially noticed.

(1) *FROM HÆMORRHAGE.*

427. One of the most constant, of course, is that resulting from hæmorrhage. The loss of blood may have taken place from a wound, or more commonly is a result of hæmorrhoids, disease of the uterus, hæmoptysis, epistaxis, or ulcer of the stomach; or it may be caused by blood-sucking parasites (*e.g.*, *anchylostoma duodenale*).

Vital Phenomena.—These depend, of course, upon the amount of blood withdrawn. A few ounces may be taken from an adult without any noticeable difference, beyond, it may be, slight temporary pallor and a sense of giddiness and thirst. When a quantity amounting to five pounds or thereabout is lost in the human subject, as from rupture of an aneurism, death takes place suddenly (Wagner). When a lesser but still large amount is suddenly withdrawn, the pallor becomes very evident in the face, lips, hands, and other parts of the surface, and in the visible mucous membranes; the inspirations become deeper; and there is a tendency to their rising at regular intervals to a climax, and subsequently subsiding (Cheyne-Stokes' breathing). At the same time there is a feeling of giddiness, and a tendency to syncope if the individual attempt to rise. Thirst, loss of voice, dilatation of the pupils, and, in the later stages, convulsions are also notable phenomena.

Such hæmorrhages, however, if the person have been previously in good health, are not so liable to excite a protracted anæmic condition as where the hæmorrhage is in small quantity and often repeated. When such a chronic anæmia has been established, not only does the system suffer from the actual loss in corpuscles, but those corpuscles which are thrown off from the blood-generating organs are improperly formed, and deficient in colouring matter. In some instances the

anæmia, instead of improving progressively, gets worse, and ultimately proves fatal.

The *coup sur coup* injury inflicted upon the blood-preparing organs seems to deteriorate their recuperative powers in a much more serious manner than where a single large abstraction has taken place; and the anæmia, consequently, is long in being recovered from. The blood becomes so impoverished, that a state of hydræmia, with its accompanying dropsy, is often provoked.

In a person already anæmic from disease or from other causes, a loss which in a healthy person would be comparatively insignificant, gives rise to the gravest results.

In persons suffering from this truly **anæmic constitution** the signs are sufficiently well marked by the great pallor, often amounting to a greenish tint, and wax-like lustre of the skin (chlorosis), muscular weakness, palpitation, breathlessness on exertion, etc.

(2) *FROM ORGANIC DISEASE OF THE STOMACH.*

428. The resulting anæmia may be intense. The interference with the preparation of the peptones, together with the direct loss of blood from the coats of the organ, sufficiently accounts for this. The anæmia is not owing merely to a deficiency in the proportion of hæmoglobin, but there may also be a large falling off (75 per cent) in the coloured corpuscles (Coupland, No. 59, 1881, i. p. 492).

Hæmorrhage from **acute ulcer of the stomach** sometimes gives rise to extreme anæmia. Siegel (No. 219, 1885, iii. and iv.), in a case of this kind, found the number descend to 1,030,000 per cu. mm. The explanation is probably to be traced both to loss of blood and to impairment in the functions of the organ.

(3) *FROM VALVULAR DISEASE OF THE HEART.*

429. In valvular disease of the heart, there is also a liability to anæmia. In its essentially characteristic form, it is to be found when the disease has lasted for a long time, and most markedly a few months before it proves fatal.

(4) *CHLOROSIS.*

430. **Vital Phenomena.**—This is a peculiar form of anæmia which shows itself in young girls about the age of puberty. In some cases, however, the disease appears to be congenital. It is characterised by a peculiar green tint, with wax-like lustre, of the skin, hence the name (χλωρός, pale green). The disease is usually accompanied by more or less functional disturbance of the genital organs, and of those of digestion. Anæmic murmurs and palpitation and breathlessness, with peculiarly well marked muscular lassitude and menstrual irregularity, are prominent features. As in other forms of anæmia,

the *panniculus adiposus* is abundant, so that the individual may appear to be well nourished. The muscles are, however, attenuated. The decomposition of fats is decreased, while that of the proteids is increased, as shown by the additional quantity of urea excreted.

Anatomical Peculiarities.—There is usually an under-development of the sexual organs and blood-vessels. As Virchow (No. 236) has demonstrated, the uterus is small and infantile in appearance, and the *mammæ* are flattened and unevolved. The *heart* in some cases is extremely hypoplastic, and the *aorta* narrow. The other *internal organs* are pale and anæmic, and the *omentum*, like the subcutaneous areolar tissue, may be loaded with fat. The temperature as a rule is not below normal, although the patient suffers from the subjective sensation of cold. In certain circumstances, the temperature may even be raised.

431. **The Blood.**—The blood presents a pale, almost orange-red, tint, and easily escapes from a prick of the finger. It is sometimes deficient in corpuscles, sometimes not, and accordingly, the disease has been described as of two kinds. When it coagulates, it leaves a buffy coat. The peculiarity of the disease, as first demonstrated by Johann Duncan (No. 12, lv., Naturwissenchaft. Classe, 1867, 2 Ab., p. 516), is the depreciation of the gross amount of hæmoglobin disproportionately to the fall in the number of blood corpuscles.

Of thirty-two chlorotic girls, from fifteen to twenty-two years of age, in whom the blood corpuscles were counted by Siegel (No. 219, Nos. xi., xii., xvi., xxiv., 1884), there was a decrease in the number in five. In other five there was no decrease, and in the remaining twenty-two, there was a very evident decrease, ranging between 3,690,000 and 1,960,000 per cu. mm. There was a diminution of the colouring matter, however, in all cases. The following extract from a very instructive table given by him, showing the relationship of the number of corpuscles to the hæmoglobin in various anæmic states, will serve to illustrate the want of correspondence between the two.

Designation of Disease.	Per cu. mm.		Number of corpuscles per milligramme of hæmoglobin.	Quantity of hæmoglobin per corpuscle.
	Corpuscles.	Hæmoglobin.		
		Millig.		μμ gr.[1]
1. Woman.—Intense chlorosis, at commencement of treatment . . .	3,600,000	0·038	94,620,000	10·55
2. Woman.—Chloro-anæmia, at commencement of treatment on 15th January 1877	2,800,000	0·048	58,330,000	17·14
A melioration on 20th February 1877	3,300,000	0·062	53,220,000	18·78
3. Woman.—Chloro-anæmia during treatment	2,720,000	0·053	51,320,000	19·48
4. Woman.—Old chlorosis, treatment with iron for many years . . .	4,000,000	0·091	43,950,00	
5. Woman.—Essential anæmia . .	1,830,000	0·033	55,450,0	

[1] The sign μμ stands for the $\frac{1}{1000000}$ of $\frac{1}{1000000}$ of a gramme.

The *serum* of chlorotic blood, where the case is uncomplicated, differs little from that of health. The disease, therefore, is one essentially in which there is a deficient production of haemoglobin, and, from what has been said of the organs in which the impregnation of the corpuscles with this takes place, it might naturally be expected that the *spleen* and *bone marrow* would be at fault. The disease as yet, however, has not been associated with any distinct lesion of these organs.

One remarkable point in connection with it, as contrasted with pernicious anæmia, is the salutary, almost specific, effect produced in many cases by the administration of iron.

Under the use of this drug, according to Hayem (No. 40, Nov. 20, 1876), not only does the hæmogoblin increase in quantity, but numbers of new coloured blood corpuscles, paler and smaller than those of health, are noticed to appear during its administration.

Literature on Anæmia and Chlorosis.—**Ancopt:** Étude comparée de l'Anémie et de la Chlorose, 1867. **Benczur** (Hæmoglobin in): Deut. Arch. f. klin. Med., xxxvi. 1884, p. 365. **Biermer:** Corresp. Bl. f. schweiz. Aerzte, ii. 1872. **Bouchut:** Gaz. d. Hôp., xlviii. 1875, p. 146. **Bouillaud:** De la Chlorose et de l'Anémie, 1859. **Febre:** La Chlorose, 1867. **Gowers:** Lancet, 1878, i. p. 675. **Habershon:** Lancet, 1863, i. pp. 518, 557; *also*, Med. Times and Gaz., 1876, i. p. 249. **Harris** (Etiology): St. Barth. Hosp. Rep., xii. 1876, p. 307. **Hayem:** Compt. rend. Acad. d. Sc., lxxxiii. 1876, p. 307; *also*, Union méd. Par., xxiii. 1877, pp. 1026, 1037; *also*, Cong. périod. internat. d. Sc. méd., Compt. rend., Genève, 1878, p. 211; *also*, Compt. Rend. Acad. d. Sc., xc. 1880, p. 225. **Immermann:** Cycl. Pract. Med. N. Y., v. Ziemssen (transl.), xvi. 1877, p. 282. **Lepine and Germont** (Microcytes): Gaz. méd. de Par., vi. 1877, p. 218. **Litten:** Berl. klin. Wochnschr., xiv. 1877, pp. 1, 748. **Loache:** Die Anämie, 1883. **Malassez** (Cancerous): Bull. Soc. anat. de Par., lxix. 1874, p. 282. **Mantegazza:** Gaz. med. ital. lomb., iv. 1865, pp. 197, 205. **Masius:** De la Microcythémie, 1871. **Moriez:** La Chlorose, 1880. **Patrigeon et Meunier:** Arch. gén. de Méd., xxx. 1877, p. 197. **Pepper:** Phila. Med. Times, ix. 1878, p. 54. **Pollock:** Lancet, 1875, ii. p. 201. **Sanderson:** Med. Times and Gaz., 1871, i. p. 1 *et seq.* **Schulze:** Ueb. d. Chlorose, 1868. **Skene:** Med. News, Phila., xliv. 1884, p. 293. **Trousseau:** Clin. Med. (transl.), N. Syd. Soc., v. 1872, p. 95. **Virchow:** Ueb. d. Chlorose u. d. damit Zusammenhängenden Anomalien im Gefässapparate, etc., 1872. **Vulpian:** Clin. méd. de l'Hôp. de la Charité, 1879, p. 463.

(5) *PROGRESSIVE PERNICIOUS ANÆMIA.*

432. **History and Nomenclature.**—It would be quite out of place here to give anything like a complete historical record of this disease, so ponderous has the literature on the subject become; and hence all that can be attempted is to indicate some of the literary landmarks which have led up to our present knowledge of it.

The first clinical account of pernicious cases of anæmia, as distinct from anæmia in general, seems to have been given by **Addison**, who clearly described how, for many years, he had observed a particular class of anæmic cases which were not due to any very immediate and recognisable cause, and which ended fatally. He gave the disease the name of "Idiopathic Anæmia," on account of the absence of any assignable reason for its occurrence (See Addison's Collected Works, New Syd. Soc., pp. 212-213).

The name "Essential Anæmia" was applied to it by **Lebert**, who affirmed that

in the year 1853, he had seen and described the disease for the first time (See No. 107, Ap. 1876, p. 385).

In the year 1857 several cases were put on record by **Wilks** (No. 63, 1857, p. 203), and the pathological features of the disease, including the fatty heart, were described in a second paper on Addison's disease, Pernicious Anæmia, etc. (No. 63, 1859, p. 108) by the same author.

Up till the year 1868, however, the pathology of the disease had been but superficially investigated; for, since the time when Addison and Wilks had recognised its clinical features, it did not seem to have attracted much attention. In this year, **Biermer** (No. 238, No. viii. Sect. ix. 1869, p. 173) drew attention to the great frequency with which the heart, arteries, and capillaries underwent fatty degeneration in idiopathic and secondary anæmias, and to the hæmorrhages and enlargement of the spleen as accompaniments of the disease. Later on (No. 239, Jahrg. ii. No. 1, 1872), he related the history, symptoms, and pathological features of the disease in fifteen cases. He also named the disease "Progressive Pernicious Anæmia."

The condition of *fatty degeneration of the heart* which is so common a complication of the disease, was specially investigated by **Ponfick** (No. 43, Nos. i. and ii. 1873), who showed experimentally that hæmorrhage, when excessive, will cause it.

In Germany, **Cohnheim** (No. 13, lxviii. 1876, p. 291) is generally regarded as having pointed out the morbid state of the bones; but **Pepper** (No. 82, Oct. 1875) in America, and **Fede** (No. 240, vii. 1875, Nos. xvii. and xviii.) in Italy, had both described the condition of the bones in the preceding year. Researches upon the same subject were subsequently made by **Scheby-Buch** (No. 140, 1876), **Bradbury** (No. 6, 1876), and **Osler and Gardner** (No. 50, 1877).

General Vital Phenomena of the Disease.—The main distinctive points of this form of anæmia, as contrasted with others, are (1) It occurs at an age when chlorosis is not liable to be met with. (2) A large proportion of the cases are in males. (3) Its course is unaffected by the administration of iron. (4) It always terminates fatally.

The commencement of the disease can often be traced to a hæmorrhage, such as that resulting from delivery; but just as frequently there is no such assignable cause.

Subdivisions.—The disease has, accordingly, been divided by Eichorst (No. 241, p. 66) into two varieties, according as it has been preceded by some predisposing systemic influence, or not. The latter he names Essential, Primary, Idiopathic, or Progressive Pernicious Anæmia; the former Secondary, Sympathetic, or Deuteropathic (δεύτερος, second) Pernicious Anæmia, following (*a*) pregnancy and delivery, (*b*) diseases of the alimentary canal, (*c*) losses of blood and liquids, (*d*) bad surroundings, insufficient nourishment, care, and anxiety.

Connection with Leukæmia.—Cases have been recorded by Litten (No. 43, Jahrg. xiv. 1877, pp. 257, 278), Leube and Fleischer (No. 13, lxxxiii. 1881, p. 124), and Waldstein (No. 13, xci. 1883, p. 12), in which the disease was followed some time before death by leucocythæmia. Two of the cases occurred in women after childbirth, the third commenced without any appreciable cause.

The Blood.—As a rule, it is deficient in *colour*, and inclines, as in chlorosis, to an orange-red. It readily escapes from a puncture.

In extreme cases, its *watery appearance* is very characteristic, both before and after death. It has been noticed, by Broadbent (No. 193, 1875, p. 22), to have so yellow a colour that it stained the hands. Pale yellow soft clots are found in the chambers of the heart, and the *specific gravity* is low.

In one case recorded by Quincke (No. 208, xxv. and xxvi. 1880), it came down to 1028·2 and when allowed to stand, the layer of blood corpuscles which fell to the bottom of the vessel occupied only one-sixth of the whole column of blood.

Fränkel (quoted by Eichorst, No. 242, p. 37) found in one case four days before death, 11·57 parts solids in the 100 parts blood, of which 1·81 was of a nitrogenous nature (nitrogen in dry blood 15·66 per cent, ash of moist blood 0·746 per cent). In another case, he found 12·11 parts solids in 100 parts blood, and 1·83 per cent

FIG. 182.—PERNICIOUS ANÆMIA BLOOD, SHOWING EICHORST'S CORPUSCLES.

nitrogen (nitrogen in dry blood 15·10). Healthy blood contains 20·24 parts solids in 100 parts blood, and 3·27 per cent nitrogen; nitrogen of dried blood 16·17 per cent. There would thus appear to be a reduction both in the total quantity of solids and in the quantity of nitrogen.

The Coloured Corpuscles.—These are always found to be diminished in number. In one case which came under the notice of the author, the loss in their number could be observed almost daily. They have little tendency to run together into *rouleaux* when evaporation commences, and are said by Eichorst not to become crenated when dried, but only to present a wavy outline.

They are deformed, in many instances (**poikilocytes**), and among them are numerous small corpuscles (**microcytes**); but the latter, as shown by Rosenstein (No. 43, Jahrg. xiv. 1877, p. 112), Lépine (No.

243, 1877, p. 141), and Litten (No. 43, Jahrg. xiv. 1877, p. 257), are by no means constantly present.

Eichorst's Corpuscles.—The small spherical and dark-red coloured corpuscles described by Eichorst have already been referred to (Sect. 421). As stated, they do not seem to be perfectly diagnostic of the disease, although a frequent constituent of the blood.

Giant blood corpuscles or **megalocytes** are also met with, and are said by Osler to be a constant element in this disease. He regards them as imperfectly transformed corpuscles.

FIG. 183.—PERNICIOUS ANÆMIA BLOOD, SHOWING POIKILOCYTES AND MICROCYTES (×600 DIAMS.)

The blood-plates, according to Halla (No. 141, 1883, p. 198), are reduced in number.

The Leucocytes.—As before remarked, some cases of pernicious anæmia have been known to terminate in true leucocythæmia. A leucocytosis, or slight excess of leucocytes, is a common feature.

Hæmoglobin.—The gross amount is vastly *diminished*, but the **individual corpuscular value** in hæmoglobin is *increased*. In some instances it may be doubled. In ordinary anæmia on the other hand the corpuscular value in hæmoglobin is usually unaltered (Osler).

Condition of Organs after Death.—One of the main characteristics, of course, is the intensely blanched appearance of the whole body, most pronounced in the lips, fingers, heart, and brain.

The **brain** looks as if its vessels had been thoroughly washed out with water. The medullary substance presents a dead white appearance, and contrasts in a remarkable manner with the gray. It is not as a rule otherwise morbid, and is of firm consistence.

There is, as in chlorosis, an excessive amount of **fat** in the subcutaneous areolar tissue, on the omentum, appendices epiploicæ, and on the surface of the heart. The muscles, however, are generally poorly nourished.

In three cases Litten (No. 43, Jahrg. xiv. 1877, pp. 257, 278) found the muscles well developed and of a dark red colour, thus contrasting with the deeply anæmic heart.

The **heart** is almost always found to be fatty in one or other ventricle, or in both; the columnæ carneæ, and musculi papillares being the parts in which the striated appearance so indicative of the disease (Sect. 502) is most evident.

The **small arteries and capillaries** in various parts of the body are also frequently the seat of a fatty degeneration. The tunica intima is the coat which particularly suffers.

Other organs are all more or less anæmic, the kidney losing its natural red colour and becoming of a pale yellow, while the liver in certain instances is fatty, and contains much more iron than normally.

The condition of the **spleen** seems to be as yet very unsatisfactorily investigated. At times it is increased in size, but not always; and there is nothing constant in regard to its colour and consistence.

The **lymph glands** are often enlarged, and can be felt through the skin. Those of the mesentery are frequently of considerable size.

The **abdominal sympathetic** has been described as being fibrous and the nerves in the ganglia atrophied, but not as a constant occurrence.

The **urine** is sometimes albuminous, but does not present the characters of hæmoglobinuria.

The author has several times met with a peculiar **soft light-green coloured tumour** situated in the anterior mediastinum, usually attached to the posterior aspect of the sternum. It had all the appearance of a round-cell sarcoma, but had a quite remarkable green colour (chloroma). Similar tumours have been described of late by Waldstein (No. 13, xci. 1883, p. 12), who also speaks to its rarity. Huber calls it a chloro-sarcoma.[1]

The Bone Marrow.—From what has been said of the participation of the bone marrow in hæmopoiesis, it may be supposed that its condition in this disease has been keenly inquired into.

Fede and Pepper, as previously mentioned, seem to have been the first to draw attention to the morbid appearance it presents in

[1] For further information refer to Durand Fardel (No. 244, xi. 1836, p. 195), Arsu (No. 107, 1854, p. 385), and Balfour (No. 19, xli. 1834, p. 41).

many cases. The latter described the bone marrow as having a dark red colour like a fresh blood coagulum, and as containing besides blood corpuscles numerous granular cells with large nuclei.

It was Cohnheim (*loc. cit.*), however, who signalised the fact that there are numerous *immature coloured corpuscles* within it. "At the first glance through the microscope," he wrote, "one could distinguish red nucleated cells of various sizes, and elliptical or spherical in shape." He also found numerous ordinary *medulla cells* (leucocytes) and *polynucleated giant cells;* while the blood corpuscles within it were of various dimensions, the smallest of them of the diameter of mature coloured blood corpuscles.

The alterations met with in it, as a rule appear to be essentially those described by Cohnheim—a preponderance of immature coloured blood corpuscles causing a swelling and unusually intense red colour.

In many instances, however, the bone marrow has been asserted to be quite sound. Eichorst (No. 241, p. 279) makes the remarkable statement that in *all* the cases which came under his notice the bone marrow was healthy.

Neumann (No. 43, Jahrg. xiv. 1877, p. 685) and Eichorst (*loc. cit.*) are at one in supposing the lesion of the bones to be secondary. Neumann says there is nothing to show that a lesion such as that described by Cohnheim, is the cause of the disease. The lesion of the bone when it is present, seems to be very much the same as that found in medullary leucocythæmia.

Hæmorrhages.—Another feature of the disease is that of the punctiform hæmorrhages in various parts of the body, most commonly on the serous membranes covering the lung, heart, and abdominal viscera, and in the pia mater and retina. Their cause is as yet undetermined, but in all probability they may be due to the altered composition of the blood hindering a free circulation, together with the fatty condition of the terminal vessels.

Etiology.—On this aspect of the disease our knowledge is still very deficient. There is doubt as to whether in reality the morbid state of the bones is to be regarded as of primary or of secondary significance. We know pretty surely where the coloured corpuscles come from in health; we know that the corpuscles in this disease are deficient in number, and not in colour; but what we do not certainly know, is whether they fail to be generated, or, being generated, how they are subsequently destroyed.

The latest researches are in favour of their being destroyed after being formed. The author has taught for many years that they are probably dissolved by some morbid product within the blood. Hunter (No. 59, Sept. 22, 29, and Oct. 6, 1888; and No. 371) makes out that this product is of a cadaveric nature, and is absorbed from the intestinal tract. The destruction of the corpuscles takes place in the branches of the portal vein, and hence the liver contains a large excess of iron. The presence of hæmoglobin in the urine, as in other forms of blood-destruction, is not a feature of this disease, because the liver

evidently arrests the products of destruction and thus hinders their entrance into the general circulation.

Under this heading it may be remarked (let the statement be taken for what it is worth) that Frankenhauser (No. 50, 1883, xxi. p. 49) has described a small **flagellated organism**, one-tenth part the length of the long diameter of a blood corpuscle, in several instances of pernicious anæmia occurring in puerperal women. He has found these organisms, he says, in the blood of all puerperal women suffering from pernicious anæmia, but not in other puerperal women.

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LEUCOCYTHÆMIA (*Leukæmia*).

NOMENCLATURE AND HISTORY.

433. On October 19th of the year 1845, Bennett of Edinburgh described (No. 19, lxiv. p. 413) under the title of "Case of Hypertrophy of the Spleen and Liver, in which Death took place from Suppuration

of the Blood," a very remarkable case in which he had examined the body after death—a case unlike anything else which had been published up to that time. It occurred in a man aged twenty-eight, and was characterised by great enlargement of the liver, spleen, and lymphatic glands, along with an excess of colourless cells in the blood. Bennett in a later work named the disease "Leucocythæmia" (λευκός white, κύτος a cell, αἷμα blood).

The facts of this case recalled to Craigie, at that time physician to the Edinburgh Royal Infirmary, the clinical history and *post mortem* examination of another, a man in whom he had found the same appearances after death, and in which Dr. John Reid, then prosector, made out, that the "blood of the veins of the abdomen and sinuses of the brain . . . contained globules of purulent matter and lymph."

In November of the same year, Virchow published (No. 245, 1845, November, No. 780) the record of a similar case in a female aged fifty under the title "White Blood" ("Weisses Blut"). He stated that by this term he meant a condition in which "the proportion between the red and colourless (white when in mass) corpuscles was reversed, without an admixture of foreign chemical or morphological elements being recognisable." In this case the spleen was about a foot long, very heavy, dark brownish-red in colour, and hard and friable; while the heart vessels contained yellowish-green masses which in great part consisted of colourless corpuscles.

These were the cases which first drew attention to the disease, and as will be perceived, Bennett had the merit of priority in publication, although the discovery of the disease may, to all intents and purposes, be said to have been made simultaneously and independently by himself and Virchow. Virchow named the disease "Leukæmia" (white blood), and claims that he was the first to indicate the true nature of the disease, Bennett having described it primarily as a *suppuration* of the blood.

In Bennett's later works on the subject (No. 280, xii. and xiii. 1851; and *Ibid.*, xiv. 1852), he gave up the old idea of the disease being a suppuration of the blood. He criticised Virchow's designation of "Leukæmia" adversely, in that the term was more applicable to **lipomatous blood** than to this.[1]

VARIETIES OF THE DISEASE.

Leucocythæmia v. Leucocytosis.—The name, therefore, historically, did not merely signify an increase of leucocytes in the blood, but an increase which is associated with this permanent enlargement of the spleen and lymph glands, and which leads to an invariably

[1] For a further account of Bennett's observations, consult his work on *Leucocythæmia or white-cell Blood in Relation to the Physiology and Pathology of the Lymphatic Glandular System*, Edinburgh, 1852. Virchow's various monographs are contained in the *Gesammelte Abhandlungen zur wissenschaftlichen Medicin*, 1862, pp. 149-218.

fatal issue. A mere increase of a temporary nature in the number of colourless corpuscles, unaccompanied by the splenic tumour, general enlargement of the glands, or disease of the bone marrow, is known as a **leucocytosis.**

Leucocythæmia and Disease of Bone Marrow.—Since Bennett's and Virchow's discoveries, however, it has been found that occasionally a pernicious form of increase of the leucocytes in the blood is met with, in which neither the lymph glands nor the spleen are enlarged. Cases of this kind have been recorded by Virchow (No. 129, p. 199), Heschl (No. 13, 1855, p. 353), and Behier (No. 150, 1869, xcix. p. 100), and in many of them it is most probably the bone marrow which is at fault. To this variety the name **myelogenous leucocythæmia** is applied. Neumann was a strong upholder of the doctrine that the bone marrow is always diseased. This, however, is not so. Numbers of cases have been recorded of late years, in which the bone marrow was quite healthy.

Leucocythæmia and Disease of Lymph Glands.—A third variety, **lymphatic leukæmia,** was admitted by Virchow (No. 13, v. 1853, p. 83), in which the lymph glands seem to have been the starting point of the disease, and in which the spleen was little, if at all, involved. Such cases, however, are rare, the enlargement of the lymph glands being usually associated with that of the spleen, especially in the later stages of the disease.

Leucocythæmia and Disease of Intestinal Follicles.—A fourth variety has been alluded to by Virchow (*loc. cit.*) and Behier (*loc. cit.*), in which an enlargement of the lymph follicles of the intestine is the most prominent lesion.

The splenic, lymphatic, and bone lesions are, however, often simultaneously present, and the question may well be asked, whether these varieties of the disease can be classified as separate forms. There, no doubt, is evidence of increase of the colourless corpuscles in the whole of them, but is that any reason why they should be associated under the same generic designation? Increase of the colourless corpuscles occurs from a host of different causes; but no one, after having seen a case of true *splenic leucocythæmia*, would ever couple the disease with anything else. The characteristic enlargement of the spleen followed by that of the lymph glands, the enormous excess of colourless corpuscles, the diminution of the red, the peculiar aspect of the patient, and the lymphoid deposits in other organs, surely form a clinical picture which marks the disease out as something *per se*.

It may here be briefly stated that Jaccoud and Labadie-Lagrave (No. 249, xx. 1875, pp. 403-404), basing their conclusions on Ranvier's idea of the universality of lymphadenoid tissue, wherever met with, classify leucocythæmic diseases from a purely *pathologico-anatomical* standpoint. They go on the assumption that the presence of lymphadenoid tissue (His) is the true criterion of the disease, and that this tissue may be found in various parts of the body according to circumstances. *Leucocythæmia* and *adenia* are regarded by them as identical diseases, that is to say,

they are the expression of the same malady which they call the **lymphogenous diathesis.** There may be excess of leucocytes in the blood or not. They recognise (1) a lymph-glandular form with concomitant leucocytosis or not; (2) a splenic form combined with the former or not; (3) an intestinal form; (4) an osseous or myelogenous; (5) a cutaneous form; and (6) a tonsillar or pharyngeal form.

GENERAL VITAL PHENOMENA.

Apart from the physical signs produced by the alteration in size and structure of the diseased viscera, there are others which may be briefly alluded to. The disease commences *insidiously* and without any evident predisposing cause. The patient becomes anæmic, breathless on occasions, and is affected with extreme muscular lassitude. He falls off in flesh, night sweats come on, and he becomes, day by day, weaker. *Hæmorrhages into the retina* are frequently found, and *ulceration of the gums* is an occasional symptom. *Pain in the bones*, on pressure, has been signalised by Mosler (No. 13, lvii. 1872, p. 532) as a frequent symptom, and has been associated by him with a characteristic lesion of the bone marrow. *Lymphoid tumours* occasionally appear upon the skin (Biesiadecki, Ranvier, Malassez, and Debove). They seem to be composed of the same kind of lymphoid tissue as that found in other organs ensheathing the small blood-vessels. The patient usually dies in a state of *asthenia*, but sometimes the fatal issue is brought about by an intercurrent attack of pericarditis or pleurisy, or occurs from a cerebral hæmorrhage.

The *male sex* is much more frequently affected than the female, and the individual is usually well up in years.

CHEMICAL ANALYSIS.

Scherer (No. 119, ii. 325, 1852) was one of the first to make a chemical analysis of the blood in this disease, and found *hypoxanthin* (sarcine), *lactic acid*, *formic acid*, *acetic acid*, and *two bodies allied to gelatine* together with *uric acid* and *leucin* present.

Mosler and Körner (No. 13, xxv. 1862, p. 142) discovered the presence of hypoxanthin in the urine. They concluded that there was a production of hypoxanthin in the spleen, in the splenic but not the lymphatic form, and consequently, an excess of it in the blood, transudations, and secretions. They regarded its presence as a diagnostic sign. Jacubasch (No. 13, xliii. 1868, p. 196) carefully examined the urine from two females, twenty-three and thirteen years old, suffering from splenic leukæmia, with the result that he was also able to detect the presence of hypoxanthin in it as well as in the transudates of the serous cavities. He finds that other foreign ingredients are not present with anything like regularity. Ranke (No. 246) made out that the relative and absolute amount of uric acid in the urine was increased.

From 2500 grms. of liver tissue taken from a leukæmic patient, Salkowski (No. 13, lxxxi. 1880, p. 166) was able to extract a *peptone-like substance* in great quantity, together with 1·718 grm. *tyrosin*, 0·864 grm. *leucin*, 0·2426 grm. *hypoxanthin*, other *xanthin-like bodies* 0·538 grm., and small quantities of *succinic acid*, but no uric acid. He says, however, that the significance of these bodies is vitiated by the want of

extensive enough researches in health and disease. Peptone-like bodies, he remarks, had not hitherto been isolated from the liver, but, possibly, this may be due to their not having been diligently enough sought for. Tyrosin is met with in numbers of other diseases, and hence, cannot be regarded as of special import.

Salomon (No. 187, ii. p. 65), has drawn attention to the production of hypoxanthin in the blood *after death;* and the supposition that it is a *post-mortem* product might at least gain support from the analysis by Bockendahl and Landwehr (No. 13, lxxxiv. 1881, p. 561) of a leucocythæmic spleen excised by Esmarch, one hour after removal. The spleen weighed 3250 grm., and of this they took 1600 grm. to work upon. A piece of the same was immediately tested for glycogen, but with negative results. They found tyrosin to be absent, *leucin* in considerable quantity, *peptone* to the extent of 14·5 grm., *lactic acid* 0·168 grm., and *succinic acid* 0·029 grm. Hypoxanthin and uric acid were not found, and they look upon this as pointing to its production after death. It ought in justice to be added, however, that neither was it found in this case in the liver after death, which occurred six hours from the time of performance of the splenotomy, nor in the various transudates.

Tyrosin and leucin were abundant in the liver, and in the blood effused into the abdomen.

There was no peptone in the pericardial fluid, which was also free from corpuscles; and they think that, when present, it may be bound up with the colourless corpuscles of the blood.

It is possible that, as it prevents coagulation (Sect. 378), the severe **hæmorrhages** which sometimes occur in the disease may be due to it.

Albukalin.—Reichardt (No. 248, pp. 389, 392, 1870) has reported the presence of an azotised substance in the dried residue of the blood similar in composition to albukalin ($C_4H_9NO_3$), and for which he has provisionally adopted this name. Albukalin was formerly described by Theile (No. 248, iv. p. 172, 1867) as a product of decomposition of albumin.

Charcot-Robin Crystals.—When leucocythæmic blood is allowed to stand for a few hours or days, or when the organs, more especially the spleen and bones, are exposed to the atmosphere, a number of crystals gather on the surface, about whose composition there seems still to be some difference of opinion. They were first described by Charcot and Robin in the year 1853 (No. 94, v. 1853, pp. 44, 49), and since then, have been the subject of investigation by Wallace (No. 250, Ap. 1855), Charcot and Vulpian (No. 251, 1860, p. 755), Neumann (No. 14, ii. 1866, p. 507, and elsewhere), and many others.

On superficial scrutiny they appear to be delicate, regularly formed, colourless and shining crystals, and when more closely examined they become resolved into elongated octohedra. Neumann stated, that they were insoluble in cold, but were readily dissolved in hot water, and he never succeeded in recrystallising them. Alcohol, ether, and chloroform did not affect them, nor did glycerine. Acetic, tartaric, and phosphoric acids rapidly dissolved them; and hydrochloric and nitric acids, when dilute, but not when concentrated. Sulphuric acid, when very weak or very strong, destroyed them. They resisted putrefaction, and after three weeks were abundant.

They are never observed in the blood during life.

Charcot and Vulpian (*loc. cit.*) regarded them as of a proteid nature; Friedreich (No. 13, xxx. p. 382), Jaccoud and Labadie-Lagrave (No. 249, p. 411), and others supposed that they were merely tyrosine, but this view has been disputed. According to Gamgee (No. 21, p. 153), they appear to be composed of the phosphate of a base which Schreiner (No. 252, cxciv., p. 68) has discovered in semen and in the spirit in which anatomical preparations have been kept.

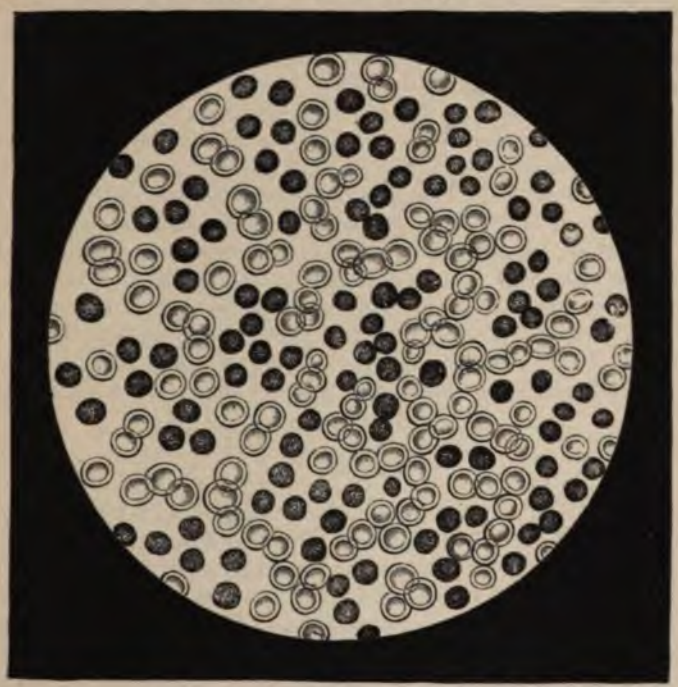

FIG. 184.—LEUCOCYTHÆMIC BLOOD (×450 DIAMS.)

THE BLOOD.

Its reaction is said to be acid (Scherer), owing to the acids, before mentioned as found on analysis, namely, formic, acetic, and lactic. Its specific gravity has been almost invariably below the normal (Bennett and Robertson).

When withdrawn from a puncture it has a grayish-red appearance, which becomes more marked after standing, so that in some cases a pus-like surface may gather upon the drop.

When seen after death in the heart and large vessels, it sometimes resembles the contents of an abscess cavity (Virchow), and often contains soft grayish-yellow coagula, especially in the right ventricle and pulmonary artery. The blood, when removed, has a dull grayish-pink appearance, and when it is allowed to stand in a tall vessel, a purulent layer gathers on the surface. The whole of the colourless corpuscles,

however, do not rise to the surface. It has a peculiar mawkish, pus-like odour in some cases, which is also common to the whole of the viscera. The number of leucocytes proportionally to the red corpuscles in normal blood may be stated at from 1 : 350 to 1 : 500 (1 : 422 down to 1 : 811, Halla). In leucocythæmia, they may be of equal number. This is brought about in a two-fold manner, firstly, by a diminution of the red, and secondly, by an addition to the number of the colourless. In a case related by Toenniessen (No. 253; see Penzoldt, No. 43, 1881, xxxii.), where they were counted by Hayem's apparatus, the red sank as low as 705,000 per cu. mm. The colourless corpuscles vary in size, some of them being smaller than those of health, and possessing a single nucleus; but the majority are large and prominent objects. The small corpuscles, as previously mentioned, were considered to be more frequent in lymphatic leukæmia. It is said, that they do not exhibit amœboid movements (Laking, Klein, Cavafy), a statement which is probably true of some of them. The coloured corpuscles are not only diminished in number but sometimes there is a large proportion of microcytes among them. Heuck (No. 13, lxxviii. 1879, p. 475) gives the history of a case in which a short time before death large numbers of these suddenly made their appearance.

THE VISCERA.

Spleen.—The organ is very much enlarged, and may occupy the whole of the left side of the abdómen. Its weight may run up to between 16 and 18 lbs. The diaphragm, or some surrounding viscus, is by no means infrequently adherent to it. It is notched anteriorly, a diagnostic sign of considerable importance. The capsule is sometimes considerably thickened, more particularly on its outer aspect. On section it has a dull gray, greenish-gray, or reddish-brown colour, and the surface may appear as if in a state of diffuse suppuration. The odour, before referred to, is particularly strong in this organ. Its consistence is, however, firm and unlike that of an organ becoming disintegrated by suppuration. The Malpighian bodies have been found absent in all the cases which have come under the personal notice of the author.

Of sixteen cases in which the spleen was found to be enlarged, Bennett (No. 254) recorded that it weighed above 9 lbs. in 3; above 5 lbs. in 2; above 3 lbs. in 2; above 2 lbs. in 4; and nearly 1 lb. in 1 case. In 4 cases it was not weighed. The greatest measurements were 16½ in. long by 9½ in. broad.

In some of them the texture was dense, in others natural, and in a third class, more or less soft and pulpy. In a few instances, he describes yellow masses of degenerated tissue, evidently infarctions.

Microscopic Structure.—In the most characteristic cases of leucocythæmia, it appears almost as if the lymph-adenoid structure of the Malpighian body had extended throughout the whole organ. Its

substance is literally crammed with colourless cells, with only a very delicate reticular stroma between them. The tissue, in fact, looks like a lymph-gland in a state of inflammation.

The *sinuses* appear to be all destroyed, and the coloured blood corpuscles, which ought to be present in the pulp, are almost absent. Blood pigment is described as of occasional occurrence, but is not invariably present.

Bones.—In those cases where the bone marrow is diseased, the lesion seems to be of two kinds. In one class of cases the marrow of the short bones is swollen, red, and congested; in another, again,

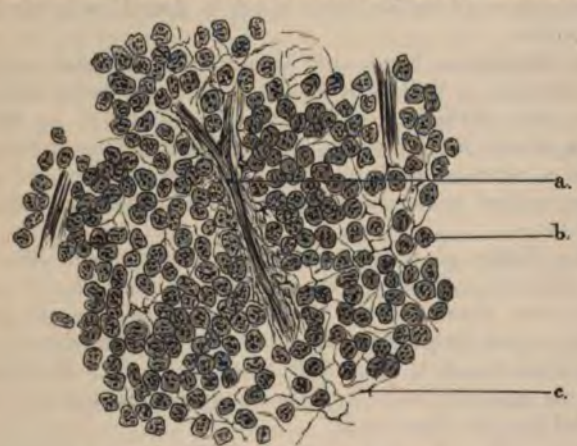

FIG. 185.—LEUCOCYTHÆMIC SPLEEN (×300 DIAMS.)
(*a*) Trabecula; (*b*) leucocytes filling the reticular tissue (*c*). (Hæmatoxylene and Farrants' solution.)

it is pale and anæmic, and of a purulent aspect, as in suppurative osteo-myelitis. Although the morbid appearances are most evident in the short and flat bones, yet those which are hollow are not exempt.

In a case of lienal-lymphatic-myelogenous leukæmia, described by Ponfick (No. 13, lxvii. 1876, p. 367), the medulla of the ribs was found to be very pale, pure gray coloured, or passing into a grayish-red, and of soft, almost diffluent, consistence. Both tibiæ were much enlarged, and the medullary tissue projected from the spaces in the spongiosa. The colour of the medulla of the epiphyses was grayish-red, while the immediately adjacent parts of the diaphyses were of a dark red or violet hue.

In a second case, he describes the bones as well shaped, and the medulla of the sternum as of a violet-red colour, and, in consistence, very much like splenic pulp. The medulla of the ribs was highly developed, of a pale grayish-red colour and very soft, while the cortical part was thin. The medulla of the diaphyses of the tibiæ, as well as their upper epiphyses, showed a delicate gray-red to a violet tint; while the lower epiphyses had a sulphur yellow colour, with, here and there, spots of a deep red hue.

In some cases the sternum may yield a pus-like liquid on pressure, its cancellous spaces being distended with it, and their walls rarefied.

On microscopic examination, the marrow is found to be engorged with cells of much the same character as those met with in health, but in the parts which are gray and purulent, the number of colourless cells, as compared with those which contain hæmoglobin, largely preponderates. The colourless cells are of various sizes, and possess one or more nuclei.

Lymph Glands.—The most swollen are those of the neck, the mesentery, axillæ, and groins. They present an iron gray colour, with occasional points of redness, like extravasations, scattered through their substance. Small nodular masses are sometimes seen in them. On microscopic examination, their tissue is found to be choked with colourless cells.

Other Organs.—The *liver* is usually much enlarged, and throughout its substance, as well as in that of the *lungs*, *kidneys*, and, occasionally, the *brain* (Friedländer, No. 13, lxxviii. 1879, p. 362), small **tumours,** almost like tubercles, are abundant. They usually vary in size from a mustard seed up to a large pea. They are gray and gelatinous, and of round shape; and are particularly abundant in the liver and lung.

Opinion differs as to the nature of these tumour-like deposits. Virchow (No. 13, v. 1853, p. 43) held that they are to be considered as of the same nature as the tissue which causes the enlargement of the glands, a true *lymphadenomatous deposit;* and Ranvier (No. 255, p. 245) has done much to lend this theory support. Rindfleisch (No. 256), on the contrary, looks on them simply as *areas into which leucocytes have exuded from the blood-vessels.*

Bizzozero (No. 13, xcix. 1885, p. 378) agrees with Virchow as regards their nature. He says that karyokinetic figures are to be found in those colourless cells which constitute the tumours, but not in those within the vessels; and he holds that they must therefore be of a different nature. The tumours are, he thinks, new formations of colourless blood corpuscles, or, as Virchow expresses it, "a kind of new lymph gland in the midst of an organ which otherwise contains nothing of the kind."

The solitary follicles and Peyer's patches, in certain instances, are much swollen, and, as previously indicated, sometimes constitute the main lesion.

Tumours, similar to those of other organs, are occasionally present upon the walls of the **respiratory passages,** and in the **skin.** They are not nearly so common on the **peritoneum** as in tuberculosis, although cases have been recorded in which they were present.

ETIOLOGY.

When we come to the etiology of the disease, difficulties arise on all sides. Is the condition of the blood, or that of the blood-forming

viscera, to be regarded as the starting point of the disease? At the present day, the answer will be almost universally in favour of the latter, and probably rightly so.

Then another important question follows the solution of the foregoing. Granted that the blood-forming organs are at fault in the first instance, what is the nature of the error? Do they throw off an excess of leucocytes, or do they simply fail to convert those which are circulating through them into coloured blood corpuscles?

The reply in this case must be regarded as uncertain, but, all things considered, is in favour of the latter view. Not only are the colourless corpuscles more abundant than in health, but the coloured are decreased in number. We have seen that the probable function of the spleen and bone marrow is to impregnate the leucocytes with hæmoglobin, and to bring about the other transformations necessary to convert them into the homogeneous non-nucleated hæmocytes.

In this disease, the spleen and bone marrow become loaded with leucocytes, but the means for their metamorphosis is evidently not forthcoming. The organs which should secrete the hæmoglobin fail to perform their functions properly, and hence an excess of untransformed leucocytes accumulates in their interstices and in the circulating blood, while at the same time the number of coloured corpuscles necessarily sinks.

This seems the most feasible view, but it should be remembered that other theories have been held deserving of careful consideration.

When we inquire still further what it is that unfits these organs for the discharge of their proper functions, we are totally at sea. Call it a neurosis, or what you will, we do not seem to be one step nearer the truth in this respect than we were over forty years ago, when Bennett and Virchow described their first cases.

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LEUCOCYTOSIS.

434. **Definition.**—By this is meant, as before stated (p. 509), a mere temporary increase of the colourless corpuscles.

Fallacy.—In accurately counting the leucocytes contained in blood, it is necessary to take the blood from the same part of the body, and otherwise to ensure that the conditions as to time of withdrawal, diet, and so on, are as nearly as possible alike in each observation. Erroneous results are sure to be obtained if these points are not attended to.

Thus Tarchanoff and Swaen (No. 4, ii. 1875, p. 324), on carefully counting the white corpuscles, found that the number in blood taken from different parts of the body was hardly in two places alike. The blood of the inferior thyroid artery in a dog contained 11,900 per cu. mm.; that of the jugular vein 8600. In another dog these numbers were augmented. The blood of a collateral branch of the crural artery contained 4690; that of the crural vein 8900; that of the tibial artery 12,500; and that of the jugular vein 13,200. In order to test the effect of obstructed circulation in the blood of the veins, they applied a ligature to the crural, and in a few moments the blood of its collateral branches contained 18,700 colourless corpuscles. Section of the sciatic nerve increased the number in the crural vein from 8200 to 14,100. They concluded that there is no general rule as to the relative number of leucocytes in the arteries and in the veins.

Conditions under which it occurs.—**Age** makes a considerable difference as regards the number to be found in the blood (see Sect. 373). **Loss of blood** also increases their number. A very marked leucocytosis has been often noted **in dying persons** as the agony is approached. Litten (No. 43, Jahrg. xx. 1883, p. 405) has shown that, a few hours before death, there is almost always a

sudden accession to the number of leucocytes in individuals suffering from various diseases. The relative number of colourless to coloured may come to be as high as 1·5. He accounts for the condition on the supposition that, either the colourless fail to be converted into the coloured, or that, as the force of the circulation diminishes, the leucocytes accumulate in greater numbers in the peripheral zone of the blood column of the small vessels, and hence escape in excess when these are punctured.

As previously indicated (Sect. 367), there is considerable difference of opinion as to whether they are increased or not after **food**; but it is pretty generally admitted that, as a rule, the colourless corpuscles are more or less augmented in **pregnancy, typhoid, tuberculosis,** and more particularly in **local inflammations** and in **pneumonia.** The increase in these diseases bears no direct relationship to the intensity of the fever, although their number usually decreases as the fever subsides.

Number.—Most recent authorities regard them as diminished when under 4000 and as increased when above 10,000 per cu. mm.

CHAPTER XXXIII

THE BLOOD—(*Continued*)

DIABETES MELLITUS

435. ALTHOUGH, strictly speaking, diabetes mellitus cannot be considered as, radically, a disease of the blood, yet, seeing that the latter is so much involved during the course of the malady, it may perhaps be preferable to consider it under diseases of the blood than elsewhere.

NOMENCLATURE.

Diabetes (διαβαίνω, to pass over) is described as of two kinds, namely, diabetes mellitus and diabetes insipidus. Where the urine is discharged in increased quantity, where it more or less constantly contains grape sugar in much greater abundance than in health, where other bye products of tissue change are added to it, and where, as a rule, the disease ultimately proves fatal, the condition is known as **Diabetes mellitus.**

Diabetes insipidus is the term employed to designate a simple increase in the quantity of water discharged by the kidneys.

The term **Glycosuria** or **Mellituria** is that adopted to express the temporary presence of sugar in the urine, with or without excess of water, the disease not, as a rule, ending fatally.

HISTORY OF THE FORMATION AND DESTRUCTION OF SUGAR IN THE ANIMAL BODY.

436. The **starchy matter** taken as food is converted by the diastatic or sugar-forming ferments contained in the saliva (ptyalin) and pancreatic juice (amylopsin), first of all, into **maltose** ($C_{12}H_{22}O_{11} + H_2O$), a sugar containing one molecule of water less than glucose ($C_{12}H_{24}O_{12}$), and **dextrins.** The maltose is subsequently transformed by the intestinal juice into **glucose** or **grape sugar.** This grape sugar is almost completely absorbed by the portal vein, not by the lacteals,

and is carried up to the liver, where it in great part becomes converted into **glycogen.** Cane sugar is similarly converted into maltose.

According to Pavy (No. 59, 1883, i. p. 776), a quantity of the maltose and dextrin is absorbed as such by the portal vein, and makes its way up to the liver, where it is transformed into glycogen. He found that dextrin of low cupric oxide reducing power was converted into glycogen when brought into contact with liver and blood outside the body. The greater part of it, however, apparently first becomes transformed into grape sugar.

The **dextrins,** according to the same authority, are of various kinds, and are distinguished by their optical properties, and by their power of reducing cupric oxide. From the colloidal principle, starch, which has no cupric reducing properties, dextrins, possessing increasing cupric reducing power, are obtainable by the action of ferments, until maltose is reached, which constitutes the final product, and which possesses about half the reducing power of glucose.

If the grape sugar is absorbed rapidly, as when a large quantity is taken into the stomach of a previously fasting individual, a certain portion makes its way directly into the blood, and if the quantity thus received into the blood be in excess, it is excreted by the kidneys.

It is only during the time that sugar is being absorbed from the intestine, that the portal blood contains more sugar than the blood of other parts of the body. The hepatic vein, at other times, both when an animal is starved and when it is fed on a carbo-hydrate diet, contains more sugar than the portal does (Seegen, No. 169, xxxvii. 1885, p. 348).

The conversion by the liver of the grape sugar into glycogen, was named by Cl. Bernard (No. 257, 2d Ser., T. iv. 1873, p. 1155) its **glycogenetic function.**

The reason for this conversion of the sugar received from the intestine into glycogen is obviously, that it may thus be stored up in the liver substance, to be given off in quantity sufficient for the requirements of the system, but not in such excess as to be excreted by the kidneys.

Glycogen, according to Pavy and Gorup-Besanez, has the same formula as starch, namely, $C_6H_{10}O_5$. It can be obtained from the liver by dissolving in an alkali, precipitating the filtered solution in alcohol, and collecting the precipitate. It forms a white amorphous powder free from nitrogen, which dissolves with opalescence in water. It gives a bluish-red reaction with iodine when isolated, but a brown when in the tissues; and is converted by dilute mineral acids, and by the diastatic ferments of saliva and of the pancreas, into a body or bodies having the same power of reducing copper as grape sugar. It has strong right-sided circumpolarisation properties.

Glycogen is found not only in the liver but in many other organs and tissues, such as the kidney, pancreas, spleen, brain, the placenta in embryonal life, muscle, cartilage, and blood; but is most abundant in the liver and in muscle.

The starch and sugar elements of the food, however, cannot be the only source of the sugar in the blood, because, as originally shown by Cl. Bernard (No. 259, troisième leçon, p. 70), it is found that the blood contains abundance of it in an animal fed exclusively on flesh.

Seegen (No. 109, xxxix. 1886, p. 121) states, that, in eight dogs which he fed on a purely flesh diet, the sugar of the blood of the carotid artery amounted to 0·150, that of the portal vein to 0·141, and of the hepatic vein to 0·281 per cent; that is to say, the blood generally contained a large percentage of sugar; while the sugar of the blood of the hepatic vein was greatly in excess of that in the systemic circulation. The glycogen is also increased in the liver when the dog is fed on a flesh diet; and the conclusion, until quite lately, stood unassailed, that it is the glycogen which is the sole cause of the large proportion of sugar found, under this diet, in the hepatic vein. As shown further on, however, this view has recently been called in question.

The glycogen ordinarily present in the liver may, therefore, be derived both from the *grape sugar* absorbed from the intestine and from *peptones*. In the latter case, the albuminous molecule splits up into urea and a carbo-hydrate which is afterwards reduced to glucose (Pavy).

The glycogen which has been stored in the liver is next given off in small quantities, and was believed by Cl. Bernard to be so rapidly reconverted into sugar by contact with the blood that it could issue from the liver only in that state. The truth seems to be that the conversion takes place either in the liver or in the blood of the hepatic vein, and is effected by means of a diastatic ferment, as yet unisolated. The ferment is supposed to be a constituent of the blood, and probably is contained more abundantly in the blood of the hepatic artery than in that of the portal vein (Brunton, No. 209, v. 1879, p. 406).

It is only right to add, however, that Pavy (No. 59, 1881, ii. p. 6) has shown that glycogen may be brought into contact with blood, and kept in contact with it for some time, at a body temperature, without conversion into more than what might be characterised as quite an insignificant amount of sugar. The glycogen is subsequently recoverable from the blood. He believes (No. 59, 1883, i. p. 776) that the glucose ferment is contained in the liver. Venous blood is antagonistic to it, and, in the liver, furnishes a maltose ferment; while arterial blood supplies in the liver the glucose ferment. Hence simple venous congestion of the organ never would induce diabetes.

The liver during life contains only a small quantity of sugar, and hence it is probable that the latter makes its appearance in the blood of the hepatic vein shortly after leaving that organ. Pavy (No. 59, i. 1878, p. 707) gives the quantity in the liver of the cat, taken at the moment of death, as ranging between 0·545 to 0·056, in the rabbit 0·554 to 0·069, and in the dog 0·315 per mille. Another explanation is, that the sugar is washed out of the organ, so soon as it is formed, by the circulating blood (Flint quoted by Brunton). After death, it increases in quantity, a circumstance which lends support to this view.

The sugar formation and its discharge into the blood appear to be functions of the liver almost entirely independent of the quantity and quality of the food supply.

This transformation of the glycogen into grape sugar is known as the **glycogenic function of the liver.** The grape sugar becomes fixed and arrested in the organ and is given out little by little, to be utilised

as fuel in the system. It is destroyed in various parts of the body, probably in great measure in the muscles. Bernard supposed that it was consumed in the lungs, but this is now known not to be the case, for although a certain small proportion may become decomposed in passing through these organs, yet the muscles are apparently the parts in which it is most consumed. It has been suggested that it is converted into *lactic acid* within them, and that heat is generated during the process. The sugar in drawn blood rapidly becomes transformed into lactic acid, and it seems likely that a similar change may occur during life. It is well known that the reaction of a muscle during exercise becomes acid.

QUANTITY OF SUGAR NORMALLY PRESENT IN BLOOD.

437. Pavy (No. 59, 1878, i. p. 706) found the average to be 0·787 per mille in the dog, 0·521 in the sheep, and 0·543 in the bullock, but as the blood was taken from different parts of the body, venous and arterial, and not from any one stated vessel, these figures can be regarded as giving only an approximate estimate.

In another paper, however (No. 59, 1877, ii. p. 54), he gives the quantity in the dog as ·811, for the carotid artery, and ·798 for the jugular vein. In a second experiment, he quotes the figures respectively at ·863 and ·879; thus showing that the difference in amount between arterial and venous blood is insignificant.

Seegen (No. 188, xliii. and xlviii. 1886) has examined the blood of Man obtained by a cupping-glass in ten young healthy individuals, and finds the quantity of sugar to amount to 0·159, and 0·194 per cent. Frerichs (No. 258, p. 9) gives it as ranging between 0·12 and 0·3—on an average 0·2 per cent. In 5 kgrm. of circulating blood about 10 grm. sugar are present.

Otto states (No. 169, xxxv. 1885, p. 467) that the quantity of sugar is somewhat greater in arterial than in venous blood. From fourteen observations, he concluded, that, in the arteries of the dog, it runs between 1·10 and 1·47 per mille; while in the veins it oscillated between 1·02 and 1·29 per mille. The blood of the horse showed that the sugar was contained almost exclusively in the liquid part. The corpuscles were practically free from it. In one case in which he examined the blood obtained by venesection in Man, he estimated the quantity to be 1·47 per mille.

One remarkable circumstance is the constancy of the quantity under varying conditions of diet, etc. Thus Seegen (No. 169, xxxvii. 1885, p. 348) made out that the arterial blood of the dog, during starvation, contains the same quantity of sugar as one fed on farinaceous diet, namely, 0·157 to 0·150 per cent. When fed with sugar, or with cane sugar and dextrine, it is higher only when the blood is taken during the time of absorption from the alimentary canal, as Bleile had previously shown. Horse's blood contains an equal amount of sugar when the animal is starved, as when freely fed, the quantity amounting to 0·144 to 0·147 per cent.

Otto (No. 169, xxxv. 1885, p. 467) found that, after venesection, the quantity remains much as before; but that inanition brings about a still greater disproportion between the quantity present in the arteries and in the veins than exists in health.

FORMATION OF SUGAR FROM SUBSTANCES OTHER THAN GLYCOGEN.

438. An interesting and important inquiry in relation to diabetes, is whether the sugar of the blood is ever derived from any other source than glycogen. When an animal is starved, the quantity of sugar in the hepatic vein is not sensibly diminished. In such a case, it must of course be derived from the tissues, for the quantity of glycogen is much too meagre to continue to supply it. Is there then a possibility that it may be derived from the fats?

Seegen (No. 169, xxxix. 1886, p. 121) found that, in feeding the dog with an exclusively fatty diet, the sugar contained in blood of the hepatic vein became increased. In an average of eight observations it amounted to 0·217 per cent in the hepatic vein, to 0·128 in the carotid artery, and to 0·114 in the portal vein; while the sugar contents of the liver itself were raised from 0·5 per cent, which constitutes the normal, to 1 per cent. The quantity of sugar which enters the blood daily in a dog weighing 10 to 12 kgrm. amounts to 200 grm. He believes that the sugar is elaborated from the fat carried to the liver, and that, in starved animals, the sugar which is found in the hepatic vein is derived from the liver fat.

In pursuance of this subject, he made observations (No. 169, xxxix. 1886, p. 132) on the capability of the liver to convert fat into sugar outside the body. From forty to fifty grm. of a recently killed dog's liver were finely cut up and digested for five to six hours, at a body temperature, along with the carotid artery blood of the same animal, with addition of a vegetable oil emulsified in mucilage. Air was aspirated into the mixture so as to keep the blood arterialised. A control experiment of the same kind, with the oil emulsion left out, was carried on at the same time. A regular increase in the quantity of the sugar of from 20 to 92 per cent was found to occur in that which contained the oil, while in the other no change followed.

METHODS OF SEPARATING THE SUGAR FROM THE BLOOD.

439. The principle involved in the older methods was identical in all cases, namely, that of the dilution of the blood with a large excess of water, the precipitation of the albumins and corpuscles with some reagent, separation of the sugar containing liquid from the precipitate by filtration, subsequent washing of the precipitate with water, and refiltration. The sugar was estimated by ordinary titration methods (see vol. ii., "Urine"). The reagents employed for precipitating albumins have been various. Seegen has lately recommended heat with iron chloride and acetate of soda.

The above principle was followed by Pavy in his older method (No. 59, 1877, ii. p. 13), but since then, he has modified it in the following manner (No. 59, 1881, ii. p. 6):—

Pavy's Method.—Let 25 to 50 c.c. of defibrinated blood be poured into five or six times their volume of spirit and be well stirred together. The glucose, being soluble in alcohol, is susceptible of extraction by this liquid. It is held, however, more tenaciously by the coagulated matter than might be expected, and hence, to effect a complete removal, several washings and pressings are required. The sus-

gulum should be allowed to remain in contact with the spirit till the following day. After being boiled by the heat of a water bath, the alcohol is strained off through a piece of linen material which has been cleansed so as to be free from dressing. The coagulum is still further washed with alcohol, and subjected to forcible squeezing, while in the linen, in a suitable sized press. The residue, which by this process is converted into a dry cake, is pulverised in a mortar, mixed with fresh spirit, boiled over the water bath, and again strained and pressed. The process is repeated once more, and this, he finds, is sufficient. Thus extracted three times, there is practically no glucose left in the solid residue, and when an aqueous extract is made, it gives no cupric oxide reducing action before subjection to the influence of sulphuric acid and heat. Two extractions with alcohol might prove sufficient, if carefully made, but it is safer to use three. To prepare the alcoholic extract for testing, the mixture of alcoholic liquids is acidified with acetic acid, heated nearly to boiling-point over the water bath, and then filtered through ordinary filtering paper. It is now brought down by heat to a small bulk, and treated with an excess of crystals of sulphate of soda, with the view of causing the fatty matter, finely dispersed through the liquid, to agglomerate, so as to be susceptible of removal by filtration. Water is added to the surplus crystals of sulphate of soda, and a hot solution made, which is used for washing purposes.

QUANTITY OF SUGAR IN DIABETIC BLOOD.

440. It was said by Cl. Bernard that if the amount of sugar reached 0·25 per cent it was excreted by the kidneys. Seegen (No. 188, xliii.; also xlviii. 1886) found that the blood in persons suffering from *slight* diabetes scarcely showed any elevation above the normal in the amount of sugar, even when the urine, under a farinaceous diet, contained plenty of it. On the other hand, the quantity in the blood of eight diabetics *in whom the disease was severe*, was far above the natural standard. Under a strictly antidiabetic diet, it came to 0·192 per cent, but in the same individual under ordinary diet, 0·314 to 0·480 per cent. He regards these results as antagonistic to the theory of Cl. Bernard above referred to. The blood can evidently contain more than 0·25 per cent sugar without its being immediately discharged by the kidneys. Pavy has found the quantity higher than 0·25 per cent in diabetics.

Experimental Evidence.—The fate of grape sugar when injected directly into the circulation appears to depend a good deal on the conditions under which the experiment is conducted. When sugar is injected into the femoral vein of a dog, it is usually considered to be rapidly cast out by the kidneys, but if injected slowly into the portal vein, it is not excreted to nearly the same extent, but apparently becomes transformed into glycogen in the liver.

Moutard-Martin and Richet (No. 40, xc. ii. 1880) state that large quantities of sugar (50 grms. per kilo. weight of the animal) can be injected into the venous system without causing death, when the animal is under the influence of morphia or chloral, provided the injection be made slowly. The blood retained 25 per cent of the sugar, a considerable part of the excess being got rid of by transudation into the intestine.

V. Brazol (No. 51, 1884, Phys. Ab., p. 211) has studied, under Ludwig's superintendence, the matter of the fate of sugar artificially added to the blood. His results seem to show that the sugar is disposed of in various ways. His method consisted in injecting a large quantity of saturated solution of grape sugar, made either with a ·5 per cent common salt basis, or with pure water, into the jugular vein. He shows that there is no direct connection between the quantity of sugar which enters the blood and that excreted by the kidneys. At most, 33 per cent is got rid of through this channel, and within two and a half to five hours, the urine is usually found to be free from sugar. Two minutes after injection of large quantities, the percentage of sugar in the whole blood was only one-half to one-fourth of what it should have been according to the quantity employed, and two hours after injection it was again normal. The sugar is disposed of in the following manner: One part per cent loses itself in the tissue juices; one-quarter part in the muscles; over one part in the liver; and a three-fourth part in the kidneys. Analysis could not detect the remainder as sugar. It is probably converted into glycogen, or lactic acid, or suffers further decomposition.

441. **Alleged Fallacy in Connection with Estimation of the Amount of Sugar in Blood by the Copper-test.**—Otto (No. 169, xxxv. 1885, p. 467) draws attention to the calculation for sugar in the blood by the copper-test being faulty, in respect of the actual amount of sugar not being estimated, but merely that of the copper oxide reducing substances.

He finds that in blood there is a substance which reduces copper with facility, but which is not grape sugar. This substance is incapable of fermentation, and hence, in order to separate the two, he employs Worm Müller's method of estimation, by which the reducing capability of the liquid is tested before and after fermentation. The difference represents the sugar.

This non-fermentible reducing substance is present in arterial blood of rabbits and dogs to the extent of 0·16 to 0·58 per mille; in venous, from 0·18 to 0·72. In venous blood of Man, he found it to the extent of 0·29 per mille. It is increased in quantity after venesection, while the quantity of the sugar remains unaltered. Hence the reducing power of the blood as a whole is augmented.

After morphia and choral narcosis, there was an increase in the reducing agents owing to an excess both of the sugar and of the non-fermentible substance. After chloroform narcosis, the same excess was present, and was caused by an increase in the non-fermentible element. Seegen has drawn attention to the fact that the CO_2 obtainable by the fermentation test for sugar (see vol. ii., "Urine") never corresponds to the apparent amount of sugar present. He supposed that it was due to incomplete fermentation of the sugar, but Otto explains it on the supposition that this non-fermentible reducing substance has heretofore been estimated along with the sugar. A good deal seems to depend, however, for the accuracy of the fermentation test, upon the time allowed to complete the process. Seegen says that forty-eight hours are in some cases insufficient for the purpose.

Pavy (No. 59, 1881, ii. p. 43) refers to a substance which is left in the residue of blood from which the sugar has been extracted by his process. It is insoluble in alcohol. By the action of sulphuric acid and heat, it is converted into a compound which behaves very much in the same way as glycogen, but he is not prepared to say that they are identical.

Glycogen, according to Frerichs (No. 258, p. 6), is always to be found in the blood, both in health and in diabetes. It is present in considerable quantity in the colourless corpuscles, and consequently, is abundant in inflammatory effusions. Its presence in the colourless corpuscles may account for Pavy having discovered it in the precipitated residue of the blood.

442. The tests for grape sugar will be found in vol. ii., under "The Urine."

EXPERIMENTAL PRODUCTION OF GLYCOSURIA.

443. We have seen that in all probability there is a ferment contained in the blood, which on passing through the liver converts the glycogen into sugar. The more rapidly the blood circulates through the organ, the more glycogen is transformed. Hence any procedure which will favour the rapidity of the circulation will tend to allow an increased quantity of sugar to enter the blood, and so occasion a glycosuria.

(1) **Division of the Pneumogastrics.**—One means by which this may be accomplished is by dividing and subsequently stimulating the vagi. If the vagi be divided in a dog during full digestion, and their upper ends be stimulated with the galvanic current for from six to ten minutes at a time, an interval of an hour elapsing between the applications, the vessels of the liver undergo dilatation, the passage of blood through them becomes facilitated, and sugar appears in the urine (Cl. Bernard, No. 259, i. 1855, p. 325).

(2) **If the floor of the fourth ventricle be punctured** by a special instrument for the purpose, the urine will be found to contain sugar a few hours afterwards (Cl. Bernard). The explanation of this phenomenon is probably the same as that of the foregoing, namely, that the operation implicates the vasomotor centre and induces a dilatation of the hepatic vessels.

(3) **Section of the spinal cord** at different levels also occasions it; and, curiously, **section of a large nerve trunk** (sciatic), according to Schiff (No. 200, iii. 1866, p 354), has a like effect. Braun (No. 260, p. 411) first drew attention to the fact that *neuralgia of the sciatic* is by no means seldom accompanied by glycosuria. *Neuralgia of the fifth* has a like causal influence (Frerichs, No. 258, p. 48). Schiff (No. 261) proved that *division of the posterior roots* of the nerves arising from the cervical portion of the spinal cord induces temporary, and similar *division of the anterior roots* in the upper cervical region of the cord, permanent (paralytic) diabetes. *Lesions of the brain* such as apoplexy, concussion, embolism, and meningitis are by no means uncommonly followed by glycosuria.

(4) **Chloral, morphia, and chloroform,** all have the property of occasionally exciting a temporary glycosuria. It should, however, be remembered, in connection with the glycosuria resulting from the use of chloral, that this substance itself has a powerful reducing action on copper solution, a circumstance which, if lost sight of, might lead

to fallacious conclusions. **Carbonic oxide gas**, when inhaled, and curare and **amyl nitrate**, when injected, also cause temporary diabetes.

(5) Injection of large quantities of 1 per cent **common salt solution** into the vascular system gives rise to it (Bock and Hoffmann, No. 51, 1871, p. 550).

(6) Injection of large quantities of **grape sugar** into the empty stomach of the dog (Bernard, No. 257, 2d series, iv. 1873, p. 1066), or into the rectum of the rabbit (Bence Jones, No. 262, p. 42), also occasions a temporary diabetes. It is questionable, however, whether sugar taken in a mixed diet has any positive effect in inducing glycosuria in Man. Lehmann (No. 263, ii. p. 375) lived on a mixed diet of sugar and fat for two days without finding any trace of sugar in the urine.

(7) **Gradual constriction and occlusion of the portal vein** by a ligature is followed by glycosuria, probably from the grape sugar contained in its blood being transferred, by other anastomotic channels, directly into the general circulation. Diabetes has been noted in diseases of the liver, such as cirrhosis, in which the branches of the portal vein are compressed. Whether the diabetes is due to the impeded circulation caused by the cirrhotic bands, or to the general disturbance in the functions of the organ caused by destruction of its tissue, does not seem quite clear.

CAUSES OF DIABETES.

444. From what has been said of the condition of the blood in diabetes (Sect. 440) it seems to be pretty clear that the reason of sugar being shed by the kidneys is that it is superabundant in the blood. The disease, therefore, is not primarily one of the kidney, although that organ may become injured in time by having to discharge an unusual and abnormal function. Nor can it be regarded, in its uncomplicated condition, as essentially a disease of the blood.

The **liver** is evidently the organ that is chiefly at fault, and on seeking for a clue to the nature of its derangement in the experimental facts bearing upon the subject, by far the most important is the readiness with which a vaso-motor paralysis—that is to say, a neurosis—allowing as it does of a freer arterial circulation through the organ, will occasion glycosuria.

Granted that the starting-point of the disease is the undue readiness with which the blood circulates through the liver, there are two secondary alternatives, through the instrumentality of either of which, the sugar may be proximately accounted for:—(1) Either its **glycogenetic** function is imperfectly fulfilled and it fails to arrest all the sugar brought to it by the portal vein, thus allowing a portion of it to enter the systemic circulation unchanged; or (2), its **glycogenic** function becomes too active, from over stimulation caused by the afflux of arterial blood to it. Both of these conditions might be excited by

increased rapidity in the circulation of the blood through its vessels. In the one case, the sugar would be swept through the organ without interruption; in the other, the transformation of glycogen into sugar would be carried on too rapidly, and an excess would thus pass into the hepatic vein.

Facts seem to favour the former of these views as being the most likely. It has been actually shown by Ehrlich (referred to by Frerichs) that glycogen was found to be almost absent from the cells of small pieces of liver withdrawn from a diabetic by means of a trochar; a circumstance which lends support to the above theory. The root of the evil, however, seems to be primarily **a neurosis** excited by some abnormality in the region of the medulla oblongata or aqueduct, but what that lesion may be, is not by any means clear.

Dickinson (No. 34, 1870; No. 59, 1883, i. p. 775) has long maintained that there must be some central nervous lesion, and indeed has described a cribriform appearance of the pons, medulla, and hemispheres, due to dilatation of the perivascular spaces, together with small hæmorrhages into the same parts. Whether these actually constitute the lesion, or whether they are an effect of it, would require still further investigation.

The sympathetic has been frequently examined in this disease (Dickinson and others), but without revealing any abnormality of note. It seems, therefore, to be probable that the lesion, if lesion there be, is situated more centrally.

MORBID APPEARANCES OF VARIOUS ORGANS IN DIABETICS.

445. **The Liver**, in typical cases of diabetes, varies in appearance, and does not present any one deviation from health which can be regarded as characteristic. It has frequently been found to be *fatty*. More or less *loosening of the epithelium* in the convoluted tubes of the **kidney**, *with unusual granularity, and a tendency to desquamate*, have also often been noticed, indeed, in some cases, amounting to a *catarrhal nephritis*. The **lungs** are, from time to time, the seat of *phthisical cavities and tubercular infiltration*. The **pancreas** has been carefully examined, but nothing of much import has been found.

The above lesions may all be regarded as *sequelæ* of the disease. There is nothing to show that any one of them has to do with its causation.

As before remarked, lesions of different parts of the **nervous system** have been described. Some of these have been located (sclerosis, etc.) in the neighbourhood of the fourth ventricle, others in the hemispheres, or in the lobes of the cerebellum.

Literature on Diabetes.—**Bernard**: Revue Scientifique, 2d Serie, T. iv.; *also*, Leçons sur le Diabete; *also*, Physiologie expérimentale. **Brunton**: Reynolds' Syst. Med., v. p. 381. **Discussion**: Trans. Path. Soc. Lond., xxxiv. 1882-3, p. 328. **Dock**: Pflügers Archive, v. 1872, p. 571. **von Frerichs**: Ueb. d. Diabetes, 1884. **Harley**: Brit. and For. Med. Chir. Rev., xxxix. 1857, p. 191. **Hensen** (Glycogen): Verh. d.

physik. med. Ges. z. Würzburg, vii. 1856; *also*, Arch. f. path. Anat., xi. 1857, p. 286. **Pavy**: Proc. Roy. Soc. Lond., xxviii. 1879, p. 520; *also*, Croonian Lectures. Lancet, 1878, i. p. 483; *also*, On Diabetes. **Philpot**: Diabetes Mellitus, 1884. **Richardson**: On Diabetes. **Saundby** (Sudden Death in): xv. 1884, p. 148. **Schiff**: Unters. üb. Zuckerbildung, 1859. **Seegen**: Wien. Med. Wochnschr., Nos. 43, 48, 1886. **Tiegel** (Glycogen Ferment): Pflügers Archive, vi. 1872, p. 249; *Ibid.*, vii. 1873, p. 291. **Traube**: Arch. f. path. Anat., iv. 1852, p. 109. **Trousseau**: Clinique méd. (transl.) N. Syd. Soc., iii. 1870, p. 491. **Unschuld**: Berl. klin. Wochnschr., xxi. 1884, p. 408. **Wilks**: Med. Times and Gaz., 1884, i. p. 78.

Literature on Sugar in Blood.—**Abeles**: Med. Jahrb., Wien., iii. 1875, p. 269. **D'Arsonval**: Gaz. hebd. de méd., xxiv. 1877, p. 581; Compt. rend. Acad. d. Sc., lxxxviii. 1879, p. 753. **Bernard (Cl.)**: Gaz. méd. de Paris, v. 1876, p. 208. **Bleile**: Arch. f. Physiol., 1879, p. 59. **Cazeneuve**: Compt. rend. Acad. d. Sc., lxxxviii. 1879, p. 595. **Dastre**: De la Glycémie asphyxique, Paris, 1879. **Ewald**: Berl. klin. Wochnschr., xii. 1875, p. 689. **Pavy** (Quantitative Determination): Med. Press and Circ., xxii. 1877, p. 1; *Ibid.*, xxvii. 1879, p. 359; Lancet, 1881, ii. pp. 5 and 43. **Picard** (Cl. Bernard's Method of Estimation): Compt. rend. Acad. d. Sc., lxxxviii. 1879, p. 755. **Seegen**: Arch. f. d. ges. Physiol., xxxiv. 1884, p. 388; *Ibid.*, xxxvii. 1885, p. 348, 369; *Ibid.*, xxxix. 1886, p. 121. **Otto**: Arch. f. d. ges. Physiol., xxxv. 1884, p. 467. **v. Brazol** (Excretion of Sugar in Excess from the Blood): Arch. f. Physiol., 1884, p. 211.

LIPÆMIA or PIARRHÆMIA (λίπος, πῖαρ, *fat*).

446. It has long been known that the serum of blood may be of a *milk-like whiteness.* The condition was familiar to Hewson (No. 230, p. 82), and to Hunter (No. 128, iii. p. 55). The former mentions the case of a young woman who was bled twelve times within six months, and in whom the serum was every time as white as milk. He refers to many previously recorded instances of this condition, and describes several other cases. Numerous cases have since then been described by Christison, Virchow, Coote, Foster, Sanders and Hamilton, Gamgee, Starr, and others (see Bibliography). It is caused by the presence of a chyle-like emulsion of *fine oil globules*, with a large proportion of a *precipitated albuminous substance.*

The blood, when withdrawn during life, has a raspberry-cream-like appearance, and when allowed to stand, separates into a milk-white stratum superficially, and an opaque reddish layer underneath. If dropped on a flat surface, the same white layer shows itself, so that it may present more the aspect of milk than blood. Very much the same appearances are noticed when the blood is withdrawn from the heart or blood-vessels after death. In one case which lately came under the author's notice, the whole of the mesenteric and gastric veins, and those of the brain, looked as if injected with some white opaque substance.

When a drop is examined immediately after removal from the living subject, or within twenty-four hours after death, the globules of oil are seen to be very minute; but after the blood has stood for from forty-eight to sixty hours, they tend to run together so as to form larger globules, and the previously white stratum assumes a slightly pink colour.

In Diabetes.—Most of the recorded cases have occurred in diabetics, although the condition has been noticed in other individuals as well. When lipæmia is associated with this disease, the blood and viscera have

the chloroform-like odour described under *Acetonæmia*. It is not present merely after a meal, but continues quite independently of the food supply.

In Health.—The serum of the blood of many animals after a meal presents a milk-like whiteness. Hewson states (*loc. cit.*, p. 89) that the blood of a goose, when withdrawn four hours after a meal of oats, presented this appearance, and he correctly attributed it to oil.

Cause.—Nothing of a satisfactory nature has as yet been made out regarding it.

Literature on Lipæmia.—**Babbington:** Todd's Cycl. Anat. and Phys., i. p. 422. **Bertrand:** Arch. gén. d. méd., xv. 1827, p. 98. **Buchanan:** Lond. Med. Gaz., i. 1844, p. 11. **Chowne:** Lancet, 1839, ii. p. 936. **Christison:** Edin. M. and S. Journ., xxxiii. 1830, p. 274. **Coote** (in Diabetes): Lancet, 1860, ii. pp. 232, 258. **Foster (B.):** Brit. Med. Journ., 1878, i. p. 78. **Fraser and Logan:** Edin. Med. Journ., xxviii. 1883, p. 199. **Gamgee:** Physiol. Chem., 1880, p. 171. **Kastner:** Ueber die Natur des weissen Blutes, 1832. **Sanders and Hamilton:** Edin. Med. Journ., July 1879, i. p. 47. **Schmiedts:** Von einem Manne bey welchem Milch aus einer geöffneten Ader geflossen. Auserl. med. chir. . . . Abhandl. d. röm kais. Akad. d. Naturf., Nürnb., iii. 1756, p. 186. **Speek:** Arch. d. Ver. f. wissensch. Heilk., 1846, p. 232. **Starr:** New York Med. Rec., May 1, 1880. **Stuart:** Philosophical Trans., ix. 1832, p. 193. **Tatham:** Lancet, 1835, i. p. 373. **Virchow:** Ges. Abhandl., 2te. Ausg., 1862, p. 138. **Zaccarelli** (Pneumonia with L.); Transl., Lancet, 1836, ii. p. 173.

ACETONÆMIA.

447. **Historical.**—In the year 1857, Petters (No. 221, 1857) drew attention to the fact that the *breath* and *urine* of diabetics had a peculiar **ethereal odour** which he ascribed to **acetone**. Kaulich (No. 221, lxvii. 1860, p. 58) confirmed these observations, and detected acetone not only in the course of diabetes, but in various other diseases, especially those of the stomach. In his opinion, it was evolved from the fermentation of grape sugar in that organ. Betz (No. 134, 1861), and Cantani (No. 264, xxiii. 1864, p. 610) continued the inquiry, the latter summing up and supporting the conclusions of the preceding observers.

Odour.—The ethereal odour of the breath above referred to, is a very remarkable feature of diabetic patients. It is sometimes so powerful that it can be readily detected throughout a large chamber. It is perceptible in the viscera after death, more especially after they have been kept for a day or two. Indeed, the stomach and abdominal viscera frequently do not exhale the characteristic chloroform-like odour at the examination, but have, on the contrary, a sour-beer-like smell. If, however, they be placed in a close vessel for twenty-four hours, and if, after this time, the cover be suddenly removed, the odour will be perceived in almost any case of diabetes, even where it has not been present during life or at the autopsy. It exactly resembles that of pure acetone.

Acetone, as obtained by the destructive distillation of acetate of lime, has the formula $CO\left\{\begin{matrix}CH_3\\CH_3\end{matrix}\right.$. It is an ethereal liquid lighter than water; it boils at 133° F.; and burns with a luminous flame. It is

easily miscible with water. Jaksch (No. 54, 1865; No. xxviii.), by distilling a very large volume of urine, found that it is, to a small extent, a normal constituent.

(1) *Lieben's Test.*—Treat the distillate, say from urine, with solution of iodine in iodide of potassium. A yellow precipitate of iodoform crystals is thrown down.

Legal's Test.—Add to the distillate a small quantity of solution of caustic soda, followed by solution of sodium nitro-prusside. A red colour should be forthcoming if acetone is present, which does not disappear on subsequent addition of acetic acid, but changes to a purple.

Diaceturia.—Some years after the above referred to discovery of acetone in the blood and urine, Gerhardt (No. 54, 1865) found in a patient suffering from diabetes, that the urine stained of a red colour with perchloride of iron, and he averred that this was due to its containing *aceto-acetic-ether*. Aceto-acetic-ether decomposes readily by heat, or by the action of acids, into acetone, alcohol, and carbonic acid.

Later on, it was shown by Deichmüller (No. 20, ccix.), and Tollens (*Ibid.*), from researches made on the urine of diabetics in Ebstein's clinic, that this substance contained in the urine, which Gerhardt supposed to be aceto-acetic-ether, was in reality *aceto-acetic-acid*, and Jaksch (No. 187, vii. p. 487) demonstrated that without doubt aceto-acetic-acid is a frequent constituent of diabetic and other urine. When aceto-acetic-acid is administered to dogs, acetone is found in the urine, and in the urine of diabetics acetone and aceto-acetic-acid are usually present together. It has therefore been suggested that acetone, when found in the urine along with aceto-acetic acid, is merely a product of decomposition of the latter.

Dreschfeld (No. 6, 1886, ii. p. 362) states that the red reaction obtained in a number of cases which came under his notice was due to aceto-acetic acid.

Frerichs (No. 91, vi. p. 1; No. 258, p. 117), indeed, discovered that aceto-acetic acid, when administered to Man by the mouth, did not pass over unaltered in the urine, but was decomposed into acetone and other products. Albertoni (No. 104, xviii. 1884, p. 236), on the other hand, states that it passes over unchanged if the reaction of the urine be alkaline, whereas, if the urine be acid, it becomes destroyed, and acetone appears in the urine.

Such cases are now described under the designation of **diaceturia**. They are characterised by the breath having a strong acetone odour, and by the urine containing acetone and giving a red reaction with perchloride of iron, this reaction being probably due to the presence of aceto-acetic acid.

Literature on Acetonæmia.—**Albertoni:** Arch. f. exper. Path. u. Pharmakol., xviii. 1884, p. 218. **Cantani:** Gior. Veneto di sc. med., xxiii. 1864, p. 610. **Edes** (Diabetic Coma): Boston Med. and Surg. Journ., cx. 1884, p. 495. **Foster (B.):** Brit. Med. Journ., 1878, i. p. 78. **Kaulich:** Vrtljschr. f. d. prakt. Heilk., lxvii. 1860, p. 58. **Kien:** Gaz. med. de Strasb., vii. 1878, p. 85. **Kruszka:** Ueber Acetonämia, 1873. **Kussmaul:** Glasg. Med. J., vi. 1874, p. 485. **Lancet** (Special Article), May 1878, i. p. 689. **Naumann** (in Phthisis): Verhandl. d. naturh. Ver. d. preuss Rheinl. u. Westphal., xx. 1863, p. 8. **New Tests for Acetone:** Med. News, Phila., xlv. 1884, p. 162. **Rupstein:** Ueb. d. Auftreten d. Acetons b. Diabetes mellitus, 1874.

Diabetic Coma.

448. Diabetics frequently die from a peculiar group of symptoms included under the above term. The individual is, as a rule, suddenly seized with difficulty of breathing, followed by drowsiness, which terminates in deep coma and death. The breathing has a peculiar panting character like that following the division of the vagi. The air enters the chest freely, but does not aerate the blood. An intermission of the symptoms for a few hours or days is sometimes noticed, but the second attack usually proves fatal. Of a total of fifty-three diabetics dying in Guy's Hospital during a space of ten years, Taylor (No. 6, 1883, i. p. 775) found that thirty-three died comatose. In ten of them, the coma supervened in the course of pneumonia or phthisis. No doubt, persons die comatose when the subjects of diabetes from various complications, but by far the most remarkable cases are those in which there is no ulterior cause for the coma in the shape of a pneumonia, or disease of the kidneys, apoplexy, etc.

Varieties.—Dreschfeld and Frerichs recognise various forms of diabetic coma. The former (No. 6, Oct. 29, 1881, and Aug. 21, 1886) divides such cases into three groups. Those belonging to the first are characterised by *drowsiness* soon passing into coma; those of the second class are distinguished by symptoms which resemble *alcoholic intoxication*, such as staggering gait, incoherent and thick speech, an excited state of the nervous system followed by drowsiness and coma; while the third group includes the largest number of cases, namely, those in which the *dyspnœa* is a marked symptom, and is followed by coma. Both the breath of the patient and the urine exhale an odour like that of acetone, and the urine contains aceto-acetic acid. (See Sect. 447.)

Pathology.—Kussmaul (No. 140, Aug. 1874, p. 1), on observing the peculiar phenomena of diabetic dyspnœa and coma, was led to the conclusion that they must be ascribed to some profound alteration of the blood, and concluded, as Peters (*loc. cit.*) had previously done, that the *acetone* present in the blood and urine must be the cause of it. This idea received support from Kaulich, B. Foster, and others, and up till a few years ago met with pretty general acceptance.

The chief *objection* to this theory is, that acetone, when inhaled or otherwise administered to animals, or to Man, does not call forth the symptoms of diabetic coma, but seems to have very much the effect of ethylic alcohol. It has been exhibited both medicinally and experimentally in large doses to Man, but in no case has it occasioned any symptom of note. Nor does aceto-acetic ether or aceto-acetic acid appear to be in anywise more powerful. Albertoni (No. 104, xviii. 1884, p. 235) gave each of them in large doses to animals, without eliciting anything like the symptoms of diabetic coma, and without a fatal result.

Fat Embolism Theory.—On examining the organs of a diabetic individual with lipæmia, and dying from diabetic dyspnœa and coma, the author discovered extensive fat embolism (see Fat Embolism) in most of the organs, manifestly in the lung and kidney, and was led, with

operation of the late Professor Sanders, to advance the theory that this might explain the symptoms. Since the publication of the paper in which this view was announced (No. 19, July 1879), the author has had the opportunity of examining the organs of another very characteristic lipæmic diabetic dying with dyspnæa and coma, with like result. Starr (No. 199, May 1, 1880) has published a similar case. There is no doubt, as Dreschfeld and Kussmaul have pointed out, that there are *different forms* of diabetic coma, and it seems quite likely that when this lipæmic condition of the blood is present, the cause of the symptoms may be ascribed to the great difficulty the blood has in circulating, owing to the mass of minute oil globules and precipitated albumin contained in it. From what has already been said (Chap. xiii.) of the necessity of maintaining a certain constant relationship between the specific gravity of the blood plasma and that of the bodies suspended in it, it is only to be expected that, in lipæmia, symptoms of obstructed circulation should manifest themselves.

Method of Preparing.—Several authors have stated that they have been unable to find oil emboli in lipæmic individuals. A great deal depends upon the methods employed for hardening and staining the tissue. The globules of oil as a rule are small, more so than in fat embolism from fracture of a bone, and, consequently, might be passed over unnoticed. The lung should be hardened in $\frac{1}{4}$ per cent chromic acid solution, the other organs in Müller's fluid followed by spirit. Extremely thin sections are to be cut in the freezer, afterwards deeply stained in perosmic acid, and finally, mounted in Farrants' solution. The capillaries will then be seen to be filled with a finely granular *débris* in which the oil globules are contained. The latter can be noticed to run into larger masses and to inject systems of capillaries in particular parts, such as those on the alveolar walls and in the glomeruli of the kidney.

Negative Cases.—There are undoubtedly cases, however, in which the symptoms of diabetic dyspnœa and coma are present, and in which no white blood or fat embolism is to be seen. The pathology of such cases is as yet by no means clear, and the careful examination of the blood and organs would in all probability lead to valuable results. In a case of this nature, which recently came under the author's notice, the capillary vessels in the lung were seen to contain an unusually large number of leucocytes of great size. In some parts they seemed to have obstructed the circulation, and to have given rise to much congestion. Whether the chemical alterations the blood had suffered, were such as to unfit it to circulate leucocytes or not, was of course impossible to determine after death. The appearance was certainly remarkable, and the whole subject may well reward further investigation.

Literature on Diabetic Coma.—**Devlin**: Med. Rec. N. Y., xxix. 1886, p. 545. **Dreschfeld**: Brit. Med. J., 1886, ii. p. 358. **Foster (B.)**: Brit. Med. J., 1878, i. p. 78. **Mabboux**: Rev. d. Méd., vi. 1886, p. 759. **Quincke**: Berl. klin. Wochnschr., xvii. 1880, p. 1. **Rose**: Med. Rec. N. Y., xxix. 1886, p. 612. **Saundby**: Birm. M. Rev., xvii. 1885, p. 49.

CHAPTER XXXIV

THE BLOOD—(*Continued*)

RHEUMATISM (ῥευματισμός, *a defluxion*).

449. THE pathology of this disease is, at present, in a most unsatisfactory state, indeed, so much so, that it may fairly be asked whether we possess any pathology at all of the disease. Like most ailments of whose cause we know nothing, theories have been rife in all ages regarding it, but experimental confirmation of the validity of any one of them has as yet completely failed.

LIMITATION OF THE DISEASE.

It is questionable whether some of the subdivisions accepted by various authors can be regarded as distinct varieties of the disease. The border-land between *rheumatism* and *gout* seems as yet ill defined, so that some authors, even of late years, suppose that the one may be complicated by the other and so give rise to a so-called *rheumatic gout.*

Hutchinson (No. 264, ii. 1881, p. 92, 98) still retains the idea that rheumatism may be complicated with gout, partly from gouty deposits of urate of soda being found in and around joints showing a distinctly rheumatic character, partly from the accompanying symptoms. Garrod (No. 264, ii. 1881, p. 97), however, cannot agree with him in this, and views the two maladies as of distinct and separate origin. He calls in question the possibility of distinguishing between them by the study of their effects upon the joints.

The opinion, however, at the present day, is pretty generally accepted that the presence of uric acid in excess in the blood and tissues is indicative of gout, and that its deposition within a joint or soft tissue is proof of the gouty nature of the disease.

There is also reason to doubt the true rheumatic nature of the so-called rheumatism which follows *gonorrhœa.* Garrod (No. 264, ii. 1881, p. 97) believes that it is more closely allied to *pyæmia* than to either rheumatism or gout. His grounds for this opinion are,

that urethral rheumatism has an essentially purulent tendency, not infrequently ending in suppuration of the joint or in the formation of adhesions.

STATE OF THE BLOOD.

In **acute articular rheumatism,** the blood, as pointed out by Sydenham (No. 369, p. 257), closely resembles that found in the phlegmasiæ (see Sect. 375). It contains an excess of *fibrin*, and becomes buffed and cupped on coagulating. The quantity of fibrin may amount to 4 to 10 parts per mille (Andral and Gavarret), and the clot is consequently particularly firm, the buffy layer measuring from 4 to 10 mm. thick. The *albumin* is quantitatively defective, and the number of coloured corpuscles, according to Malassez, is diminished. Clots of *ante-mortem* formation are by no means infrequently found in the heart and blood-vessels, sometimes in the blood-vessels of the brain.

It has often been asserted [primarily by Prout (No. 351, p. 81), and subsequently by Todd (No. 272) and Fuller (No. 270)] that **lactic acid** is present in excess in the blood, but such has never been absolutely proved.[1]

The serum preserves its alkaline reaction, and its solids are diminished (Becquerel and Rodier). The *urea* has been stated by Lebert to be in excess.

STATE OF THE JOINTS AND OTHER INFLAMED PARTS.

It is not often that an opportunity offers itself of examining the state of the joints in acute rheumatism, but in such cases in which an inspection has been obtained after death the appearances were very much like those of acute inflammation of the joint from other causes. The whole of the **soft tissues** of the joint seem to be implicated. The **synovial membrane** is thickened and injected; its epithelium is shed, and at parts it seems to be infiltrated with inflammatory exudation. In still more advanced cases, it may almost come to resemble a granulating surface, with minute blood extravasations upon it, and pus may actually be discharged into the cavity of the joint. As a rule, however, suppuration is rare, although an excess of synovial liquid will usually be met with. This liquid presents a thick viscid appearance with numerous inflammatory cells in it. It has commonly the ordinary colour of synovia, but in some examples is deeply stained with blood. It possesses an alkaline reaction and contains much albumin and fibrin (Senator).

The **cartilages** are not much altered, unless as a sequela to the rheumatic affection, when they may ulcerate and the whole joint become disorganised. The **epiphyses of the bones,** with the exception of a little undue vascularity, are not much involved.

The **surrounding fibrous textures** of the joint are usually in-

[1] Consult Gaglio on lactic acid, *Arch. f. Anat. u. Physiol.*, Phys. Ab., 1886, p. 400.

filtrated and œdematous, and an inflammatory cellular exudation pervades them, as in the case of the synovial membrane. In other tendinous structures affected by the inflammation, an analogous condition is met with.

Apart, however, from the mere joint and tendon manifestations of acute rheumatism, there are others affecting vital parts of even greater importance. These are comprised in **inflammations** of the **endo-** and **pericardium,** and of the **pleura.** For particulars regarding them, the reader is referred to the chapters on the circulatory and respiratory organs.

THEORIES AS TO ITS CAUSE.

(1) **Cold.**—A very old, and at the present day still prevalent opinion is that acute rheumatism is due to exposure to cold and damp. It is generally supposed that exposure to cold checks the natural secretory functions of the skin, and so causes the retention of effete matters in the blood. Fuller (No. 270, p. 2 *et seq.*) strongly opposed this doctrine, pointing out that in many cases there is no such history, and that a period of ill health generally precedes the attack for several days, thus indicating some previous disturbance in assimilation or metabolic interchange.

(2) **Presence of Lactic Acid.**—Lactic acid is a constant constituent of the urine in acute rheumatism, and, as previously referred to, has been supposed to be in superabundance in the blood. Such, however, has never been proved to be the case. It is only right, however, to state that Senator (No. 206, xvi. 1877, p. 29) rather favours the view that if the secretion from the skin be suppressed by cold, or otherwise, lactic acid may accumulate in the blood, and possibly might account for the symptoms.

The prevalent notion (Headland, No. 271) in former times was that the lactic acid was not oxidised and thus mechanically accumulated in the blood. Fuller (*loc. cit.*) was strongly in favour of this view, which alone of all theories hitherto propounded, he held, was reconcilable with admitted facts.

Latham (No. 6, 1880, ii. p. 977) explains the probable presence of lactic acid differently. With others, he regards the inhibition during life of the chemical changes which the tissues would ordinarily suffer, were they dead, as being controlled by the influence of certain nervous centres. If these centres be deranged, as he assumes they are in rheumatism, lactic acid would form, would accumulate in the muscles, and thence would be absorbed into the blood.

(3) **Organismal Theories of the Disease.**—These have not been wanting, and at the present day micro-organisms of various kinds have been alleged to be productive of the malady.

Maclagan (No. 273) looks upon acute rheumatism as of a miasmatic nature, closely allied to marsh fever. He draws a parallel between the beneficial action of salicylic

acid in the one, and quinine in the other; and regards the beneficial influence of the former as due to its germicidal properties.

Hueter (No. 274) traces the entrance of a micrococcus into the blood through the sweat ducts of the skin, and this, he thinks, may be the cause of all the mischief.

Petrone (No. 49, 1886, ii. p. 289), by withdrawing the liquid from a joint in acute rheumatism, was enabled to isolate a micrococcus from it which he holds is identical with that found by Klebs in rheumatic endocarditis.

Guttmann (No. 49, 1886, ii. p. 289) found, on making cultures of the liquid from a joint from the pericardium, and from a kidney abscess of a boy who died from acute rheumatism, that the only organism obtainable from them was *Staphylococcus aureus*, the common organism of suppuration, and that this was present in abundance.

Literature on Rheumatism.—**Brieger** (Connection with Nervous Disease): Berl. klin. Wochnschr., xxiii. 1886, p. 149. **Bucquoy**: Gaz. d. hôp., liv. 1881, p. 810. **Friedländer**: Verhandl. d. Cong. f. innere Med., Wiesb., iv. 1885, p. 403. **Fuller**: Brit. Med. Journ., 1868, *also* on Rheumatism, Rheumatic Gout, and Sciatica, 1852. **Gaglio** (Lactic Acid in Blood): Arch. f. Physiol., 1886, p. 400. **Garrod**: Reynolds' Syst. of Med., vol. i. **Handfield Jones**: Med. Pres. and Circ., 1868. **Homolle**: Rheumatisme, N. dict. de méd. et chir. prat., xxxi. 1882, p. 548. **Howard**: Syst. Pract. Med. (Pepper), ii. 1885, p. 19. **Maclagan**: Rheumatism; its Nature, its Pathology, and its Successful Treatment. **Pagnier**: Essai sur l'étiologie du rheumatisme articulaire aigu, 1884. **Quenstedt**: Zur Aetiol. der Rheumarthritis acutus, 1886. **Riedel**: Ueb. den akuten Gelenkrheumatismus, 1869. **Senator**: Cycl. of Pract. of Med., v. Ziemssen (transl.), xvi. 1877, p. 3. **Vogel**: Rheumatismus u. Gicht. Virchow's Handbuch, 1854.

Rheumatoid Arthritis.

(*See* Diseases of Bone and Joints).

Gout (Fr. *goutte*; Lat. *gutta*, a drop).

DEFINITION.

450. The disease is a more or less general one, influencing many organs and tissues, and manifesting itself externally in chalk-like deposits of urate of soda in the small joints of the toes and fingers, in the tips of the ears, and in other localities. The part which suffers most frequently is the metatarso-phalangeal joint of the great toe. The term Podagra (πούς, a foot, and ἄγρα, seizure) is applied, strictly speaking, to this local manifestation of the disease in the foot, but loosely, is employed synonymously with gout in its wider acceptation.

CAUSE.

Undoubtedly, as first demonstrated by Garrod (No. 34, xxxi. 1848, p. 83; No. 275; and No. 209, vol. i.), the immediate cause of the symptoms is an excess of uric acid in the blood. For some reason, this is not entirely eliminated by the kidneys, but is deposited in the form of concretions in the joints and in other parts of the body.

SOURCES OF URIC ACID.

451. Uric acid ($C_5H_4N_4O_3$), in the form of urate, is a constant constituent of the urine of mammals, and, in very small quantity (0·05 per mille or less), also occurs in the blood. Being but sparingly soluble in water (1 in 14,000 parts cold water, and 1 in 1800 hot—Hoppe-Seyler), it exists in both of these situations in combination with alkalies, forming salts which are also only sparingly soluble in water, although more soluble than the pure acid.

In the cells of the kidney and elsewhere, according to Bence Jones (No. 262, 1867, p. 109), a process of oxidation occurs in health; other acids are thereby produced, and the alkaline urates are likewise transformed into more acid urates which pass out of the kidneys to the amount of 6 to 10 grains of uric acid daily.

The salts which are found in the urine are accordingly **acid urates**, chiefly of ammonium ($C_5H_3(NH_4)N_4O_3$), sodium ($C_5H_3NaN_4O_3$), and potassium, the last being in the same relation to the acid as the sodium in its corresponding salt (Hoppe-Seyler). The salt which it forms with lithia is the most soluble, hence probably the beneficial effect of this substance in eliminating uric acid when administered medicinally.

Uric acid is an important constituent of the urine of *reptiles*, where it appears to take the place of urea in excreting nitrogen. It is also abundant in the urine of *birds*. It is present only in very small proportion in the urine of *herbivora* (Garrod), but is in quantity in that of *carnivora*.

There seems little doubt that it is to be regarded, ultimately, although not immediately, as a product of oxidation of albuminous substances; and is, after urea, the next most important means of removing nitrogen from the system. The **quantity** shed in the urine increases with the taking of food, and decreases with hunger.

Bence Jones (No. 65, Pt. ii. 1849, p. 235) found the amount excreted in the urine to vary in the following manner:—

			Sp. gr.
Before food (mixed diet) . .	from 0·048	grains per 1000 grains of urine,	1026·3
	to 0·17	,,	1023·1
After food it varied . .	from 0·39	,,	1021·0
	to 0·92	,,	1031·1
On Vegetable Food—			
Before food, ...	0·049	,,	1024·0
After food, ...	0·636	,,	1026·2
On Animal Food—			
Before food, ...	0·049	,,	1024·8
After food, ...	0·77	,,	1029·9
After three days of animal food only	1·022	,,	1027·8
,, ,, vegetable ,,	1·010	,,	1025·6

Lehmann (quoted by Garrod) made a number of experiments on his own person in reference to the influence of diet upon the excretion of uric acid. He found that:—

On a strictly vegetable diet he passed in 24 hours			15·5	grains of uric acid.	
On a mixed diet	,,	,,	17	,,	,,
On a strictly animal diet	,,	,,	21·5	,,	,,

Although an animal *diet* thus, apparently, has the effect of raising the quantity excreted, yet it cannot be the only cause of the presence of uric acid, for, as pointed out by Latham (No. 276, p. 7), the carnivorous lion and tiger excrete little uric acid, but abundance of urea, while in the urine of the equally carnivorous python and boa there is no urea, but abundance of uric acid. The diet which, in one class of animals, produces *urea*, in another class, gives rise to *uric acid*.

There are good grounds for believing that the waste in the *metabolism of muscle* and other albuminous tissues is another source of uric acid. Its quantity in the urine is augmented by exercise, and during the crises of fevers a copious discharge of urates frequently occurs.

RELATIONSHIP OF URIC ACID TO UREA.

452. It is a notion which is pretty widely entertained that uric acid represents nitrogenous waste in a less highly oxidised state than when in the form of urea.

Bence Jones (No. 262, 1867, p. 125) argued that, just as every grain of starch taken as food passes through the stage of sugar, so almost every grain of albuminous substance that enters the blood, sooner or later, in its way out, passes through the stage of uric acid, and if thoroughly oxidised, escapes as urea, carbonic acid, and water.

There are several facts which seem to lend support to the idea:—

(1) It has been found (Frerichs and Wöhler, No. 20, lxv. p. 335) that on feeding an animal with uric acid, the urea discharged by the kidneys increases while the uric acid is not augmented.

(2) Bartel's experiments (No. 140, i. 1865, p. 13) went to show that in all disturbances to the free interchange of gases in the lung, the quantity of uric acid increased in the urine. Senator, however (No. 13, xlii. 1868, p. 1), was unable to corroborate these results experimentally in all cases.

(3) Reptiles (ophidians and saurians) whose respiration is languid, excrete a large quantity of uric acid, but in opposition to this, birds with rapid and free respiration do so also.

(4) The urine of newly born children contains more uric acid than that of adults, and occasionally uric acid is deposited in them as infarction-like masses.

(5) Uric acid is increased in the urine of leukæmic individuals where the oxygen-bearing coloured blood corpuscles are diminished in number. Here, however, the spleen is enlarged and is in a morbid state, and probably this may have something to do with its increased formation.

(6) As indicated by Latham (No. 276, p. 6), one of the main grounds for the hypothesis that uric acid is due to defective oxidation is, that it can be split up by means of oxidising agents into urea and other substances. Thus when oxidised by nitric acid, it is converted into alloxan and urea (Fownes, No. 247, p. 402; Charles, No. 164, p. 457),

$$C_5H_4N_4O_3 + O + H_2O = C_4H_2N_2O_4 + CO\left\{\begin{matrix}NH_2\\NH_2\end{matrix}\right.$$

Uric Acid. Alloxan. Urea.

And, further, when alloxan is boiled with a strong alkali or with baryta water, it is decomposed into mesoxalic acid and urea,

$$C_4H_2N_2O_4 + 2\,H_2O = C_3H_2O_5 + CO\left\{\begin{matrix}NH_2\\NH_2\end{matrix}\right.$$

Alloxan. Mesoxalic Acid. Urea.

Other oxidising agents such as lead dioxide, similarly convert it into urea along with allantoin and oxalic acid (Fownes, *loc. cit.*, p. 412).

$$2\,C_5H_4N_4O_3 + O_2 + 5\,H_2O = C_4H_6N_4O_3 + 2\,C_2H_2O_4 + 2\,CO\left\{\begin{matrix}NH_2\\NH_2\end{matrix}\right.$$

Uric Acid. Allantoin. Oxalic Acid. Urea.

It seems, therefore, problematical, to say the least of it, to affirm that the relationship of uric acid to urea is simply one of suboxidation. The connection between the two is, in all probability, more subtle.

Latham (No. 276) has lately thrown much light on the possible bearing of the one upon the other. His theory is briefly the following:—

Glycocholic acid, one of the acids contained in the biliary secretion, can be converted by boiling with alkalis into glycocine[1] and cholic acid (Fownes, *loc. cit.*, p. 622).

$$C_{26}H_{43}NO_6 + H_2O = C_{24}H_{40}O_5 + CH_2\left\{\begin{matrix}NH_2\\COOH\end{matrix}\right.$$

Glycocholic Acid. Cholic Acid. Glycocine.

The same decomposition occurs in the alimentary canal, and after the acid has served its purpose in digestion, the glycocine is absorbed into the circulation to be converted into urea and eliminated by the kidneys. It is probably carried directly to the liver by the portal vein, and he is led to believe that among the numerous metabolic events which occur in the hepatic cells, the formation of urea from it and similar bodies may be ranked as one.

It is not correct, however, to say that the whole of the glycocin is transformed into urea. A portion of it is eliminated as a constituent of uric acid. In bringing this about, the glycocine apparently combines with urea, or the immediate antecedent of urea, in the liver, the conjugation of which by the gland would produce either hydantoic acid or an acid he refers to as containing two molecules of CONH.

These dehydrated would be converted respectively into hydantoin.

$$CO\left\{\begin{matrix}NH-CO\\ \quad\quad |\\NH-CH_2\end{matrix}\right.$$

or into the substance

[1] Glycocin, glycocol, or glycin, $C_2H_5NO_2$ is a decomposition product obtained by the action of acids and alkalis upon albuminous and albuminoid substances such as glue, gelatin, and fibrin. It is generally regarded as being amido-acetic acid.

$$\begin{array}{l} CO\left\{\begin{array}{l} NH - CO \\ NH \qquad | \end{array}\right. \\ CO\left\{\begin{array}{l} \\ NH - CH_2 \end{array}\right. \end{array}$$

If it be hydantoin which is formed in the liver, then on arriving at the kidney it must be conjugated with biuret ($C_2H_5N_3O_2$) to form ammonium urate.

$$\underset{\text{Hydantoin.}}{CO\left\{\begin{array}{l} NH - CO \\ \qquad\quad | \\ NH - CH_2 \end{array}\right.} + \underset{\text{Biuret.}}{\begin{array}{l} CO\left\{\begin{array}{l} NH_2 \\ NH \\ NH_2 \end{array}\right. \end{array}} = H_2O + \underset{\text{Ammonium Urate.}}{C_5H_3N_4O_3 \,.\, NH_4}$$

If the latter substance, it would be conjugated with urea and be excreted as ammonium urate.

$$\underset{\text{Urea.}}{CO\left\{\begin{array}{l} NH_2 \\ NH_2 \end{array}\right.} + \begin{array}{l} CO\left\{\begin{array}{l} NH - CO \\ NH \qquad | \\ NH \,.\, CH_2 \end{array}\right. \end{array} = H_2O + \underset{\text{Ammonium Urate.}}{C_5H_3N_4O_3 \,.\, NH_4}$$

He regards the former combination as more likely to take place in the system than the latter. If, from any cause, the elimination of urate of ammonia by the kidneys were hindered, a portion might be retained in the blood and, meeting with soda in the blood, be converted into sodium urate, the form in which it is deposited in gouty joints.

STATE OF THE BLOOD.

453. According to Garrod (*loc. cit.*) the **fibrin** undergoes the same variations as in other inflammatory diseases. When a patient is suffering from an acute attack, it may increase up to 4, 5, or 6 parts in 1000, the augmentation being in proportion to the intensity of the inflammation; but in chronic gout, it may remain in its normal proportion. He does not regard the amount of fibrin as bearing any constant proportion to the disease, but merely as depending upon the amount of local inflammation. It may therefore be buffed or cupped, on withdrawal, or it may present no abnormal feature.

The **serum** appears to be usually of lower specific gravity than in health, but in cases of acute gout occurring in robust subjects this is not so.

It always contains **uric acid** in the shape of **urate of soda**, which salt can be obtained from it in a crystalline form. In *healthy blood* there is a mere trace of uric acid, but in *gout* it may amount to from 0·050 up to 0·175 grain per mille or even more. It diminishes in quantity or seems to disappear when decomposition of blood drawn during life has set in.

The urea is said to be sometimes increased in gouty blood, but is diminished in the urine, hence showing, in all probability, that there is some difficulty in elimination from the kidney.

Oxalic acid is also frequently present.

METHOD OF DETECTING EXCESS OF URIC ACID DURING LIFE.

454. A cantharides blister ought to be applied to the skin, not over an inflamed joint, but at some distance from it. When a bleb has formed, it should be tapped with an aspirator and the liquid be received in a shallow flat glass capsule. To this add acetic acid of medium strength ($\frac{28}{100}$) in the proportion of six minims to each fluid drachm of serum. When the two are well mixed, introduce one or two ultimate fibres of unwashed huckaback or other linen fabric, which should be depressed with the point of a glass rod. Set aside in a cool place, with a dry atmosphere of gentle warmth, until the serum is almost dry. If uric acid is present, it will crystallise on the thread in the form of rhombs, and may be examined with a low magnifying power (Garrod).

The amount of uric acid in *healthy* blood is so small that it cannot be recognised by the thread test. Hence this test comes to be an important aid to diagnosis.

PATHOLOGICAL ANATOMY.

455. The anatomical lesions chiefly consist in the *deposition of urate of soda in the joints and ligamentous or other fibrous structures.* The small joints, such as the *metatarso-phalangeal*, or the *metacarpo-phalangeal*, are most frequently the seat of these deposits, but the *elbow* and *knee* are also sometimes implicated. Of all the joints of the body the **metatarso-phalangeal of the great toe**, as before stated, is that in which the inflammation first shows itself. Many explanations have been attempted to be given of this, all of them more or less unsatisfactory. The **helix of the ear** is another favourite seat.

The **affected joint**, in an acute attack, becomes hot, red, swollen, and painful, and when the disease becomes chronic, chalk-like masses of urate of soda and lime, or **tophi**,[1] are found in the ligamentous tissues around it. They are also sometimes seen in the helix of the ear and elsewhere. The skin becomes attenuated over them, and may finally give way, allowing the chalk-like mass to protrude.

When the joint is examined, its **cartilages** are usually found to be infiltrated with a plaster-like deposit of urate of soda. It is almost colourless, and may sometimes resemble an efflorescence or encrustation on the surface. Garrod, however, states that there is always a thin boundary layer of cartilage superficially.

There is not the same tendency to destruction of the cartilage as in

[1] Schroeder v. d. Kolk (quoted by Wagner, No. 211, p. 578) found the tophi from the fingers and other parts of a gouty patient to contain a large proportion of urate of lime.

some forms of rheumatism. When the urates are dissolved out, the cartilage may often not present any very marked abnormality, even when examined microscopically. In other cases, however, the cartilage becomes eroded. The more chronic the case, the greater is the amount of the deposit. The deposit seems to avoid the **vascular fringes** of the synovial membrane; it is particularly in parts poorly supplied with blood that it finds a suitable nidus. The **contents** of the joints are usually thick synovia, sometimes with a flake of fibrin in it.

In chronic cases of gout, the **kidney** shows in many instances most marked evidence of cirrhosis. It was named by Todd the "gouty kidney" on that account. It is often wasted down to one-half or even one-third of its normal size (*see* "Kidney").

There seems little doubt that the deposition of the urates in the joint or other texture is the **cause** not the effect of its inflammation.

THEORIES ON THE CAUSE OF THE ACCUMULATION OF URIC ACID IN THE BLOOD IN GOUT.

456. There are of course several possibilities—

(1) **Decreased Solubility.**—A plausible theory was that which was advanced by Garrod, namely, that the blood from *increased acidity* becomes less capable of maintaining the urates in solution. It has met with some acceptance from pathologists such as Cohnheim and Senator, but it seems doubtful as yet whether it can be seriously entertained.

(2) **Increased Formation of Uric Acid.**—It seems more likely that there is an actual *increase in the quantity of uric acid* formed.

Latham accounts for it on these grounds. As previously explained (Sect. 452), he regards the liver as naturally acting upon the **glycocine** absorbed from the intestine by the portal vein, by which the greater part of it is converted into **urea.**

Suppose, from some cause, this metabolism of glycocine be interrupted (as in the interrupted metabolism of starch or glucose in diabetes), there would then be in the gland two substances, glycocine and urea, which in the manner before explained, would be transformed into urate of ammonia and soda.

It is easy to see how derangements of the liver from over-feeding and the other acknowledged dietetic causes of gout, might readily interfere with the action of the organ in converting glycocine into urea, and result in the excessive formation of uric acid instead. Gout ("poor man's gout"), however, is a disease of the under-fed as well as of the over-fed, and he explains such cases by supposing that some change localised in the medulla oblongata or spinal cord, or in both, so modifies this function of the organ that the metabolism of glycocine into urea is imperfectly accomplished. The heredity of gout, he thinks, might thus be explained.

Physicians have long entertained the tropho-neurotic theory of gout. The doctrine was originally enunciated by Cullen, and more recently Duckworth (No. 6, 1881, i. p. 463) has revived it.

(3) **Failure in Function of Kidney.**—It is possible, however, that uric acid is not only produced in increased quantity, but that it

fails to be speedily removed by the kidneys. The amount passed in the urine during an attack of gout is small, and the kidney, in chronic cases, is almost always in an advanced state of disease. It is a question as to whether disease of the kidney alone, as suggested by Garrod, would not be sufficient to occasion an increase of uric acid in the blood. *Ligature of the ureters* in birds and reptiles causes a speedy deposit of urates in the tissues, but in mammals this operation is not followed by any such effect.

It is possible that in a first attack the powers of the kidneys to excrete the effete material may still be uninjured, but that, as in diabetes, the constant removal of uric acid in such great quantity, causes in time a deterioration in their structure; and that, consequently, in chronic cases, there is not only an increased production, but a diminished outflow of the obnoxious substance.

There is a peculiar tendency to the accumulation of uric acid in the blood and tissues of those who suffer from **lead poisoning,** but as yet its cause remains unexplained.

Literature on Gout.—**Adams:** Rheumatic Gout, 1873. **Atkinson:** Practitioner, xxvi. 1881, p. 415. **Barlow:** Cycl. Pract. Med., Tweedie, i. 1845, p. 332. **Duckworth:** Brit. Med. Journ., 1881, i. p. 463; Brain, iii. 1880, p. 1. **Durand-Fardel:** Union Méd., xxxvi. 1883, pp. 42, 65. **Ebstein:** Deut. Arch. f. klin. Med., xxvii. 1880-1, p. 1; *also*, Eng. transl. by J. E. Burton, 1886; Med. Press. and Circ., xxxix. 1885, p. 1 *et seq.* **Fothergill:** Gout in its Protean Aspects, 1883. **Gairdner:** On Gout; its History, its Causes, and its Cure, 1849. **Garrod** (Gout, Rheumatism, and Bright's Disease): Med. Chir. Trans., Lond., xxxi. 1848, p. 83; *Ibid.*, xxxvii. 1885, p. 49; *also*, A Treatise on Gout and Rheumatic Gout, 1876; *also*, Art. in Reynolds' Syst. Med., i. **Hood:** A Treatise on Gout, Rheumatism, and Allied Affections. **Hutchinson:** Tr. Internat. Med. Cong., Lond., ii. 1881, p. 92. **Jaccoud and Labadie-Lagrave:** Goutte. N. dict. de méd. et chir. prat., xvi. 1872, p. 552. **Meldon:** A Treatise on Gout and Rheumatic Gout, Lond., 1886. **Mendelson:** N. Y. Med. Journ., xliv. 1886, p. 146. **Pathology of Gout:** Brit. and For. Med. Chir. Rev., ci. 1873, p. 46. **Saundby:** Med. Times and Gaz., i. 1881, p. 32. **Senator:** Cycl. Pract. Med. v. Ziemssen (transl.) xvi. 1877, p. 107. **Sydenham:** A Treatise on Gout. **Trousseau:** Gout, Lectures on Clin. Med., N. Syd. Soc., 1871. **Virchow** (Demonstration of Gout Preparations): Berl. klin. Wochnschr., xxi. 1884, p. 75.

PURPURA AND SCURVY.

457. These two diseases appear to possess a certain bond of relationship, but so little is known of their pathology that this view has but meagre foundation in fact. They are both accompanied by hæmorrhages, and it is chiefly on this account that the belief in their affiliation has received so general assent.

PURPURA.

458. **Definition.**—Under this heading are comprised chiefly two affections of whose identity many pathologists are as yet sceptical. One of these is **purpura simplex,** in which minute petechiæ upon the skin are the chief external signs of the disease; the other is **purpura hæmorrhagica, morbus maculosus Werlhofii,** or

hæmophilia, in which the hæmorrhages are much more extensive, and occur not only on the skin, but on internal parts.

In **purpura simplex** the extravasations are very small and are found either upon the lower extremities alone, or upon all the extremities along with the abdomen or breast. They do not disappear on pressure, and are unattended by itching of the skin. After lasting for a variable time, they disappear. The disease does not usually prove fatal.

In **purpura hæmorrhagica,** however, the disease is much more formidable, and ends fatally by no means infrequently. The hæmorrhages take place into the skin and mucous membranes, and an escape of blood from the latter in the form of *hæmoptysis*, *epistaxis*, or *hæmaturia*, is not uncommon. They also occur upon the different serous membranes, and into the substance of several internal organs. In the kidney they form *wedge-shaped masses*, and similar deposits may sometimes be seen at the periphery of the lung. Those in the skin are either petechiæ, petechiæ conjoined with vibices (*vibex*, a wheal), or livid stripes and patches. They are red coloured at first, but in course of time become livid or purple. Hæmorrhages are readily caused by any slight injury of the surface. The *gums* are sometimes ulcerated, but not swollen as in scurvy (Atkinson).

The pathology of this disease is still obscure. The hæmorrhages have been explained by a fatty degeneration of the small vessels, but such observations are unreliable.

Ceci (No. 104, xiii. 1881, p. 461), on inoculating the blood of a woman—who died with extensive purpuric hæmorrhages in various parts of the body, high fever, delirium, albuminuria, and hæmaturia—into the conjunctival fornix of rabbits, found that a disease of a like kind, accompanied by hæmorrhages, could be excited, which proved fatal in a few days. The disease could be transferred from one animal to another by inoculation.

It is questionable, however, whether the disease communicated may not have been merely the result of septic contamination. Gaspard (No. 277, ii. 1822, p. 1; *Ibid.*, 1824, iv. p. 1) long ago demonstrated that hæmorrhages were produced in animals when putrid substances were introduced into their systems.

Cheyne (No. 192, 1884) has found the vessels in the neighbourhood of the hæmorrhages, in two instances of idiopathic purpura hæmorrhagica, plugged with **micro-organisms** in masses. He holds these to be peculiar, from the fact that they form *colonies within the vessels*, a variety of conformation assumed only by the typhoid and anthrax bacilli.[1] He supposes that the occlusion of the vessels gives rise to the hæmorrhages. In other two cases, however, in which he subsequently examined the organs, he failed to find any micro-organisms, an observation which lends support to the suspicion that the term *purpura* includes several diseases of unlike causation.

There is no reason for supposing that the **fibrin** of the blood is decreased in quantity.

Literature on Hæmophilia or Purpura Hæmorrhagica.—**Assmann**: Die Hæmophilie, 1869. **Austin** (Resumé): Canada Med. Rev., iii. 1874-5, p. 549. **Bannister**: Suppl.

[1] See also cases reported by Russell with examination by Cheyne, No. 6, 1882, ii. p. 414.

v. Ziemssen's Cycl. Med., 1881, p. 785. **Ceci:** Arch. f. exp. Path. u. Pharmakol., xiii. 1880-1, p. 461. **Dunn:** Am. J. Med. Sc., lxxxv. 1883, p. 68. **Futterer:** Zur Casuistik. d. Haemophilie, 1877. **Grenaudier:** Contribution a l'étude de l' Hémophilie, 1882. **Holloway:** Cincin. Lancet and Clinic., xv. 1885, p. 68. **Immermann:** v. Ziemssen's Handbuch d. Spec., Path., etc., xiii. 1876, p. 415. **Kidd:** Med. Chir. Trans., Lond., lxi. 1878, p. 243. **Koch (C.):** Ueb. Haemophilie, 1867. **Lapeyre:** Recherches sur la Nature de l'Hæmophilie, 1867. **Legg:** A treatise on H., etc., 1872; *also*, Lancet, 1881, ii. p. 999; *also*, Trans. Path. Soc. Lond., xxxiii. 1881-2, p. 412; Trans. Path. Soc. Lond., xxxvi. 1884-5, p. 488. **M'Caw:** Dub. J. Med. Sc., lxxxi. 1886, p. 507. **V. Meurers:** Die haemorrhagische Diathese, etc., 1873. **Momberger:** Beitrag zu Lehre v. d. Haemophilie, 1862. **Pepper:** Phila. Med. Times, xii. 1881, p. 109. **Reinert:** Ueb. Haemophilie, 1869. **Simon:** Recherches sur l'hemophilie, 1874. **Walker:** Brit. Med. Journ., 1882, i. p. 605. **Werlhof:** Disquisitio medica et philologica de variolis et anthracibus, 1735. **Woelky:** Ueb Haemophilie 1868. **Woodbury:** Phila. Med. Times, xvi. 1885, p. 913.

SCURVY (Scorbutus).

459. Whatever the ultimate cause of this disease may be, there is no doubt that **hæmorrhage** is one of its most marked features. The effusions take place into the *skin*, and later on, into deeper parts such as the *periosteum* and the *tissues in the vicinity of joints.* The *swellings* which are seen so frequently around bone, appear to be in great part caused by hæmorrhage along with a certain amount of inflammatory effusion. The *swelling of the gums* seems to be mostly due to the latter cause.

The **skin** also assumes a harsh dry and discoloured appearance, with a tendency to desquamation of the cuticle.

The blood does not show any abnormality which can be detected on microscopic examination, but when analysed, is said to have presented certain deviations from health. The analysis made by Andral (No. 278) seemed to point to some amount of decrease in its fibrin forming properties. Busk, and Becquerel and Rodier ("Du Sang dans le Scorbut," in No. 247), however, were unable to confirm this; in a few instances, they found it to be increased.

Garrod (No. 280, January 1848), founding on the facts that, in a diet which occasions scurvy, potash salts are in small proportion; that the disease is alleviated by the administration of antiscorbutic remedies containing the substance in large quantity; and that the blood and urine contain less potash than in health, endeavoured to trace the cause of the disease to deficiency in the potash of the blood. Ralfe's researches (No. 59, 1877, June 16, and July 21) confirm those of Garrod. He regards a deficient alkalinity of the blood as a primary factor in the development of the disease. This diminished alkalinity is occasioned in the first instance, by an increase in the acid salts in the blood (chiefly urates), and finally by the withdrawal of salts having an alkaline reaction (chiefly alkaline carbonates).

Busk gave the following as the proportion of the various constituents of the blood in scurvy in three cases.

	1st Case.	2nd Case.	3d Case.	4th (Heal. Blood).
Water . . .	849·9	835·9	846·2	788·8
Solid constituents .	150·1	164·1	153·8	211·2
Fibrin . . .	6·5	4·5	5·9	3·2
Albumin . . .	84·0	76·6	74·2	67·2
Blood corpuscles .	47·8	72·3	60·7	133·7
Salts. . . .	9·5	11·5	10·9	6·8

A later analysis made by Chalvet (quoted by Wales) is as follows:

	Scorbutic Blood.	Healthy Blood.
Water	848·492	772·225
Solid matters	151·508	220·775
Dry clot	140·194	209·000
Albumin	72·304	68·717
Fibrin	4·342	2·162
Globules	63·548	138·121
Extractive matter—by absol. alcohol . .	10·312	8·013
,, —by ether	1·002	1·300
Ash of clot	3·000	5·691
Peroxide of iron of globules	1·060	2·259
Potassium of globules	0·329	0·625

Literature on Scurvy.—**Becquerel and Rodier** (Blood): Chimie pathologique, 1854. **Busk** (Blood): See Ref. in Simon's Animal Chem., Syd. Soc., i. 1845, p. 315. **Buzzard**: Reynolds' Syst. Med., i. **Cheadle**: Brit. Med. Journ., 1872, ii. p. 520. **Duchek**: Pitha's Handbuch, i. Ab. 2, 1869. **Hirsch**: In his Handbuch d. historisch-geographischen Path., 1881. **Immermann**: Cycl. Pract. Med., v. Ziemssen (transl.), xvii. 1878. **Ralfe**: Lancet, 1877, ii. p. 81; *also*, An Inquiry into the General Path. of Scurvy, 1877. **Wales**: Article "Scurvy," Ashurst's Internat. Encycl. of Surg., i. 1882.

URÆMIA.

460. **Definition.**—By uræmia is understood that combination of symptoms resulting from the retention within the blood of the excrementitious substances naturally excreted by the kidney.

General Vital Phenomena.—The typical phenomena exhibited during life are usually ushered in by certain initial signs or *prodromata*, such as mental apathy, insomnia, cephalalgia, amblyopia, and dyspnœa. These are followed by cerebral symptoms more or less acute, and varying in character in different cases. Thus in some they may assume a convulsive type, in others it may be epileptic, tetanic, or delirious, or the patient may pass into a state of deep coma. There is also usually more or less gastro-intestinal disturbance, together with, in many cases, attacks of dyspnœa.

Pathogeny.—The condition of the kidney which accompanies these symptoms is usually one which causes more or less retention of both the watery and solid parts of the urine—such as *acute catarrhal nephritis*, or other form of Bright's disease. One acute disease of the kidney specially liable to be the cause of uræmic symptoms is *glomerulo-nephritis*, either associated with scarlet fever, or, coming on, without apparent cause. After *childbirth* there is a tendency to a form of disease

of the kidney which prevents the free excretion of urine, and this may be followed by uræmia and convulsions. What the exact condition of the kidney may be in these cases is not quite clear. The tubules will sometimes be found choked with a hyaline substance, probably albumin in an insoluble form; but this is not invariable. *Yellow fever* and *cholera* are also sometimes followed by uræmic symptoms.

Theories as to its Cause.—Some of these are founded on purely **anatomical grounds,** such as that of *cerebral œdema, cerebral anæmia, cerebral congestion,* etc. Although the brain presents a typically blanched appearance—at least in puerperal women dying with uræmic symptoms and convulsions—yet it is a question whether the anæmia can be looked upon in a causal relationship to uræmia, or whether it is a phenomenon closely bound up with the convulsive state. If the patient die during a convulsion, the brain will be found in the above anæmic condition, but, if during an interval, it does not necessarily follow that it will be so.

The **chemical theories** have met with more acceptance. They are chiefly the following :—

(*a*) *The Retention of Urea Theory.*—This has long been held to be a cause of uræmia. Christison (No. 265, p. 61) was the first to establish that the blood contained an excess of urea in Bright's disease, and since then it has been of course looked upon as a very likely cause of the uræmic state.

Feltz and Ritter (No. 267, 1882; No. 266) found it possible to inject large quantities of urea into the blood without inducing toxic symptoms, and they explain the positive results obtained by other experimenters on the hypothesis that the urea employed by them was impure, and contained among other ingredients, *salts of potash,* to which they ascribe the phenomena.

These conclusions have not been confirmed, however, by Gréhant and Quinquad (No. 200, xx. 1884, p. 393), who, on obtaining chemically pure urea, were enabled, by injecting it subcutaneously in various animals, to bring about convulsions ending fatally. The fatal dose in the rabbit is about the $\frac{1}{151}$ of the total weight of blood, and in dogs it runs between $\frac{1}{153}$, $\frac{1}{194}$, $\frac{1}{203}$. They believe that **urea** is a poison, but that in order to be effective, it must be injected in doses larger than those usually employed. On injecting a quantity of urine containing an equivalent amount of urea, however, the toxic effects were seen to be much more acute, and hence they believe that **urine** is a more powerful poison than pure urea.

(*b*) *Carbonate of Ammonia Theory.*—Frerichs (No. 138, x. 1851, p. 399; No. 268) explained the symptoms on the supposition that the urea underwent decomposition into carbonate of ammonia in the blood. He founded this supposition on the fact that urea readily decomposes into carbonate of ammonia; that carbonate of ammonia is always to be found in the blood of uræmic individuals; and that the injection of carbonate of ammonia into the blood of animals causes symptoms cor-

responding with those of uræmic poisoning. That the urea undergoes such decomposition in the blood does not, however, seem to be actually borne out by later researches.

(*c*) *Potash Salts Theory.*—Injection of human urine into a vein in animals certainly has the effect of inducing uræmic symptoms, and it comes to be a question as to which constituent of the urine is the active agent. Feltz and Ritter (No. 267, 1882; No. 266) have lately demonstrated that when the organic materials of a given quantity of urine are introduced singly into the circulation, none of them act in the same manner as the urine *in toto*. The **potash salts** contained in this quantity of urine, however, gave positive results; and on these grounds they conclude that the potassic salts are the sole toxic agents of the urine, and that it is the retention of these in Bright's disease which causes the uræmic symptoms.

(*d*) *Ptomaine Theory.*—There seems little doubt that organic alkaloids or ptomaines normally circulate with the blood, and are excreted by the kidneys. They were demonstrated in the urine by Gautier (No. 200, xvii. 1881, p. 333), and Selmi (No. 269, 1875). They exist only in small quantities in health, but are capable of considerable augmentation in disease.

Bouchard supposes that these ptomaines are in great part elaborated in the intestinal canal by the organisms of putrefaction; and favours the view that uræmia may be explained by the kidney failing to excrete them from the blood.

High Arterial Tension Theory.—The remarkable salutary effects which follow venesection in this disease have led Broadbent (No. 6, 1887, i. p. 765) to suggest that high arterial tension is to be regarded as the proximate cause of the uræmic manifestations.

Literature on Uræmia.—**Albert:** Allg. Wien. Ztng., xxix. 1884, p. 368. **Assmuth:** St. Peterbg. med. Wochenschr., 1886, iii. p. 45. **Bartels:** Cycl. Pract. Med. v. Ziemssen (transl.) xv. 1877, p. 109. **Bernard:** Contribution a l'étude, des paralysies dans l'urémie, 1885. **Christison:** Edin. Med. Jour., xxxii. 1829, p. 262; *also*, On Granular Degeneration of the Kidneys, 1839. **Feltz and Ritter** (Experimental): Compt. rend. Acad. d. Sc., 1874 and 1878; *also*, De la Urémie, 1881. **Fleischer:** Sitzungsb. d. phys. med. Soc. zu Erlangen, 1883-4, H. xvi. p. 108. **Frerichs:** Archiv. f. phys. Heilk., x. 1851, p. 399; *Ibid.*, xi. 1852, p. 88. **Gaudens:** Essai sur la relation existant entre la cause de l'urémie et son expression symptomatique, 1885. **Genestoux:** Contribution a l'étude, de l'urémie expérimentale, 1885. **Girandeau:** Arch. gén. de méd., 1886, i. pp. 84, 197; *also*, De l'Urémie. **Grehant and Quinquad:** (Urea in Blood) Compt. rend. Acad. d. Sc., xcix. 1884, p. 383. **Labadie-Lagrave:** N. dict. de méd. et chir. prat., xxxvii. 1885, p. 84. **Morat and Ortille:** Gaz. méd. de Paris, xxiv. 1879, p. 396. **Müller:** Ueber Urämie, 1885. **Osthoff** (U. and Eclampsia): Sammlung klin. Vorträge., 1886, No. 266. **Papellier:** Ueb. chem. Reizung d. Med. oblong. mit. Rücksicht auf Uraemie, 1855. **Peabody:** Med. Rec. N. Y., xxvii. 1885, p. 22. **Traube:** Berl. klin. Wochnschr., iv. 1867, p. 467. **Urémie:** Dict. encycl. d. Sc. méd., i. 1886, p. 111. **Voit:** Zeitschr. f. Biol., iv. 1868, p. 77.

Other Diseases in which the Blood is Involved.

461. In **cholera,** as shown by C. Schmidt (No. 183), the solids become relatively inspissated from the draining away of water by t

intestine. The urea is also said to be increased. The comma bacillus (Koch), which is so abundant in the intestine, has not been found in the blood (See vol. ii., "Vegetable Parasites").

In **intermittent fever** large quantities of pigment are found in the vessels leading from the spleen, and in the parts connected with them (melanæmia). It has a black colour, and is granular in form. A vegetable organism has also been found in the blood by Tomasi-Crudeli, which he considers to be the cause of the disease (See vol. ii., "Vegetable Parasites").

For the condition of the blood in relapsing fever, typhoid, septicæmia, etc., in which a specific vegetable organism is said to be present, consult vol. ii., "Vegetable Parasites." The subject of Pyæmia is described in connection with the Diseases of the Blood-vessels; and that of the Animal Parasites of the Blood under "Animal Parasites" generally.

Literature on Melanæmia.—**Arnstein:** Arch. f. path. Anat., lxi. 1874, p. 494. **Carter:** Trans. M. and Phys. Soc., Bombay, viii. 1886, p. 30. **Colin:** Traité des fièvres intermitt., 1870. **Kelsch:** Arch. de Physiol., 1875. **Mosler:** Cycl. of Med., v. Ziemssen (transl.), viii. 1878, p. 533. **Pepper** (Pigment in Remittent Fever): Proc. Path. Soc. Phila., ii. 1865, p. 181. **Planer:** Ztschr. d. k. k. Gesellsch. d. Aerzte. zu Wien., i. 1854, p. 127.

Literature on Blood in Typhoid.—**Eichorst:** Deut. Arch. f. klin. Med., xiv. 1847, p. 223. **Hayem and Gilbert:** Arch. gén. de méd., 1884, i. p. 257.

General Literature on the Pathology of Blood.—**Addison:** Lond. Med. Gaz., xi. 1850, pp. 193, 316, 488. **Andral:** Essai d'hematologie pathologique, 1843. **Andral and Gavarret:** Annales de chimie et de physique, lxxv. p. 225. **Aronssohn:** Des altérations du sang dans les maladies, 1862. **Bequerel and Rodier:** Traité de chimie path. appliquée à la méd. pratique, 1854. **Berzelius:** Trans. Med. Chir. Soc. Lond., iii. 1816, p. 198. **Brittan:** Blood Diseases and Blood Germs, 1874. **Burrows** (Croonian Lecture): Lond. Med. Gaz., xvi. 1835, p. 647 *et seq.*, xviii. 1830, p. 427 *et seq.* **Christison:** On Granular Degeneration of the Kidneys, 1839. **Davy:** Researches, Physiol. and Anat., 1859. **Flint** (Lectures): Am. Med. Times, N. Y., vii. 1863, p. 201 *et seq.* **Gamgee:** Physiol. Chem., 1880. **Gilbert and Lion** (Crit. Rev.) Arch. gén. d. méd., 1884, ii. p. 583. **Gulliver:** Hewson's works, Syd. Soc., 1846. **Halliburton** (Report on Proteids): Brit. Med. J. 1884, ii. p. 176; *also*, 1885, ii. p. 148. **Hayem:** Recherches sur l'anat. norm. et path. du sang, 1878. **Hewson:** Properties of the Blood, with Introduction by Gulliver, Syd. Soc., 1846. **Hunter (J.):** A Treatise on the Blood, Inflammation, and Gunshot Wounds. **Jones (T. W.):** Brit. and For. Med. Rev., xiv. 1842, p. 585; *also*, Am. J. M. Sc., lxxx. 1880, p. 104. **Laptschinsky:** Centralbl. f. d. med. Wissensch., xii. 1874, p. 657. **Lebert:** Virchow's Handbuch d. spec. Path. u. Therap., v. 1855, p. 61. **Prevost and Dumas:** Annales de chimie et de physique, xxiii. 1823, pp. 50, 90. **Magendie** (Series of Articles on Blood and its Diseases): Lancet, 1838-9, i. p. 41 *et seq.*; *also* REPRINT. **Quinquaud:** Chimie pathologique; recherches de hématologie clinique, 1880. **Richardson:** Brit. Med. Journ., 1865, i. p. 7 *et seq.* **Riess:** Arch. f. Anat., Physiol. u. wissensch. Med. 1872, p. 237. **Simon:** Animal Chemistry, Syd. Soc., 1845 (transl.). **Stricker:** Med. Jahrb., 1872, p. 169. **Thackrah:** On the Blood. **Williams:** Brit. and For. Med. Chir. Rev., xii. 1853, p. 465; *Ibid.*, xiii. 1854, p. 193; *Ibid.*, xv. 1855. p. 181; *Ibid.*, xviii., 1856, p. 459. **Wooldridge** (New Constituent): Proc. Roy. Soc., xxxviii. 1884-5, p. 69. **Zahn:** Arch. f. path. Anat., xcv. 1884, p. 401.

CHAPTER XXXV

THE HEART

Diseases of the Pericardium

ANATOMICAL ARRANGEMENT

462. The pericardium is a double membrane, consisting as it does of a serous and of a fibrous layer.

The **serous part** of the membrane may be regarded as the pericardium proper, and like the pleura it encloses a cavity, the *pericardial sac*. It lines the interior of the fibrous layer and is reflected over the large vessels at the base and over the surface of the heart itself. The latter reflection of the membrane is known as the *epicardium*. It is a thin fibrous expansion covered by endothelium, and beneath its cardiac reflection lies the epicardial fat together with blood-vessels, loose areolar and yellow elastic tissues, and lymphatics.

The **fibrous part** of the membrane is much coarser and more resistant than the serous.

The pericardium is abundantly supplied with *blood-vessels* from the *arteriæ pericardiaco-phrenicæ*, *arteriæ mammariæ internæ*, and from the *arteriæ mediastinæ posteriores*; the veins being chiefly branches of the *venæ pericardiaco-phrenicæ*, *azygos*, and *hemiazygos*. Lymphatics accompany the arteries, and nerve branches from the *right phrenic* and *right vagus* ramify in the parietal layer. The endothelium is said to be provided with stomata (Skworzow).

It arises below at the circumference of the central tendon of the diaphragm, whence it passes up to envelop the heart, and loses itself in the fascia surrounding the trunks of the ascending aorta and pulmonary artery. It ultimately becomes united to the deep fascia of the neck (fascia cervico-pericardiaca).

Pericarditis (*περί, around, and καρδία, the heart*).

463. **Definition.**—*An acute or subacute inflammation of the peri-*

cardium, occurring alone, or associated with endo- or myocarditis, or with both.

VARIETIES.

Although the essentials of the disease may be regarded as alike in all cases, yet, just as in inflammation of the serous membranes generally,

FIG. 186.—PERICARDITIS FIBRINOSA (×40 DIAMS.)

Shows the myocardium (M, C) and the pericardium (P, C), each provided with an organising layer (M, O, L and P, O, L), and also the fibrinous lymph (F, E, S) lying in the sac (Picro-carmine and Farrants' solution).

the disease does not run exactly the same course in every instance. Certain varieties have accordingly been distinguished as follows:

464. **P. fibrinosa.**—The disease commences with an acute hyperæmia of the pericardial vessels. The membrane becomes swollen and

infiltrated with inflammatory effusion. In the course of from thirty-six to forty-eight hours after the acute inflammation has set in, highly albuminous inflammatory liquid is poured into the sac. From this, an excess of fibrin is precipitated upon the free surfaces of the membrane. At times, the fibrin is localised, but, more frequently, the movements of the heart tend to distribute it generally.

The lymph has a pale yellow colour, and, at first, is loosely adherent to the parts it covers. In many places it can be stripped off, so as to leave a smooth surface upon which the endothelium may still be detected. It evidently gains the free surface through pores or other openings between the endothelial plates, for if seen sufficiently early, it will be found to form small villous tufts corresponding to these minute openings. Later on, the fibrin assumes a shaggy or honey-comb appearance, evidently due to the traction on the walls of the sac caused by the motion of the heart.

After the fibrin has separated from the effused liquid, a quantity of *serum* remains in the sac. In this variety of the disease, it is never large, and may be generally distributed, or be pent up in cyst-like cavities by the partial adhesion of the sides of the fibrin-coated membrane.

Sooner or later, however, the liquid is absorbed, and the walls of the sac now come into complete contact and adhere. The union as yet, however, is merely of a temporary character; but in course of time the fibrin is gradually removed, and it becomes permanent and fibrous. The means by which this is accomplished has already been described (Sect. 205).

The adhesions may be partial, or may amount to complete synechia. All such adhesions tend to impede the movements of the heart, and apparently as a consequence, its walls will often be found hypertrophied. The disease may leave a permanent thickening of the membrane.[1]

465. **P. serosa.**—The sac contains a large quantity of liquid, and only a thin layer of fibrin is to be found on the surfaces, often partially distributed.

466. **P. hæmorrhagica.**—Certain forms of fibrinous pericarditis have a tendency to cause extravasation of blood more than others. To such the above name is sometimes given. The blood mixes with the lymph, and as it coagulates, aids in accomplishing the temporary union.

467. **P. purosa.**—The inflammatory exudation not infrequently disintegrates and forms pus, or the discharge may have been purulent from the commencement. More particularly is the latter the case when the pericarditis is of a septic nature.

The sac may be filled to distension with yellow or greenish coloured pus, while some patches of half-purulent lymphy membrane may be seen still adherent to its walls. The remaining parts of the surface

[1] See case related by Broadbent, No. 6, 1881, ii. p. 745.

are sometimes red and inflamed, and in protracted cases small granulations may be found upon them.

The purulent liquid usually contains *micrococcus* in abundance, and when so, a fatal termination of the disease becomes practically a certainty.

The purulent discharge occasionally dries into a *caseous mass* or *masses*. The pericardium becomes adherent, and the fibrous connections enclose the cheesy deposits. In how far life is compatible with such a condition of the pericardium, may be a matter of question. There is of course the possibility, that the caseous residua might be absorbed, or that they might calcify. Such a favourable termination, however, is rare.

468. **P. gummosa.**—Syphilitic inflammation of the pericardium is uncommon, but there seems good reason for believing, that some old adhesions of the sac, more especially those accompanied by cheesy deposits or by fibrous myocarditis, are of this nature. Lancereux (No. 25, ii. p. 217) refers to a case which he says is the only one he has seen.

469. **P. tuberculosa.**—An acute eruption of tubercule on the pericardium is, for some unknown reason, an uncommon disease. Many of the instances of tubercular pericarditis seem to have arisen from the drying and caseation of an inflammatory effusion.

Mathieu (No. 107, 1883, i. p. 265) makes out that tubercular pericarditis occurs once in every thirty-five tubercular persons. He draws his conclusions from the statistics of Rillet and Barthez, who found it ten times in the autopsies of three hundred and twelve tubercular individuals, and of Leudet, who found eight cases in a total of two hundred and ninety-nine. Few of these cases, however, seem to have been of the nature of a miliary eruption.[1]

470. **Pericarditis from the Presence of Tumours.**—Cancerous, sarcomatous, lympho-sarcomatous, or other tumours of the pericardium are sometimes followed by inflammation. The source of the inflammation is sufficiently indicated by the presence of the particular tumour.

Pericarditis has also been noticed to accompany **scarlet fever, scurvy**, etc.

ETIOLOGY.

471. Of all known causes **acute rheumatism** stands pre-eminent in point of frequency. It may be associated, when due to this cause, with endocarditis or myocarditis, or may be uncomplicated.

Of three hundred and twenty-six persons admitted into St. Mary's Hospital during the fifteen years ending 1866, Sibson (No. 209, iv. p. 186) found that one-fifth were attacked with pericarditis, and that it was accompanied, in all but nine instances, by endocarditis. In only one-fourth of the cases was there an absence of evidence of endo- or pericarditis.

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[1] Lancereux (No. 25, ii. p. 216) gives a drawing of the miliary disease.

The precise exciting agent in acute rheumatism has not been certainly ascertained. It has been asserted (see "Endocarditis") that a micrococcus is present in the affected parts, but opinion differs on this point.

Pericarditis is also frequently an accompaniment of **septic diseases**; it is common in pyæmia. Septic organisms can be detected in the effusion. They form zooglœa masses localised in the fibrinous lymph, or, it may be, more or less generally distributed throughout the purulent contents of the sac.

In the *pericarditis of oxen*, masses of micrococcus may frequently be found in the effused lymph. Wilson (No. 19, xxxi. 1885-6, p. 924) records an instance of pericarditis in a boy where a micro-bacillus was present.

The **negative pressure of the pericardial sac**, caused by the movements of the heart, may perhaps be regarded as a condition predisposing to the disease.

Adamkiewicz and H. Jacobson (No. 50, 1873, p. 483) found, by introducing a tube rendered air-tight by means of a stilette, into the pericardial sac of the sheep, dog, and rabbit, and by connecting it with a manometer, that the pressure within the sac was negative to between three and five mm. Hg. Indeed, allowing for error in the experiment, it is probable that it may be even lower than the above.

This deficient pressure within the pericardial sac would tend to lessen the support afforded by the adjacent tissues to the vessels ramifying in the membrane, and would thus favour the expulsion of the blood constituents through their walls.

EFFECT UPON HEART AND VESSELS.

472. The accumulated liquid of a pericarditis must of course seriously impede the free play of the heart. More or less pain is experienced in many cases, sometimes amounting to true *angina pectoris*, possibly from this cause. The superior vena cava is pressed upon, and hence where the effusion is great, the vessels of the neck are often turgid.

PERICARDIAL HÆMORRHAGE.

473. **Wounds** of the heart constitute of course one comparatively common cause of pericardial hæmorrhage. A still more common cause, however, is rupture of the heart from **disease of its walls**, such as *aneurism*, softening from *atheromatous degeneration of the coronary arteries*, or *abscess*.

TUMOURS OF PERICARDIUM.

474. These are chiefly Lympho-Sarcomata, Spindle and Round-Cell Sarcomata, secondary cancers, tubercle, and hydatids.

The **lympho-sarcomata** usually arise in the anterior or posterior mediastinum, and involve the pericardial tissues secondarily. They take the form of lobulated masses, sometimes of great size, which spread into the parietal layer of the membrane, but seldom affect the visceral, nor do they generally involve the heart itself. In some cases they project into the anterior mediastinum, constituting a cap-like mass which overlaps the heart, and which might be mistaken during life for an intra-pericardial distention.

The **pure sarcomata** are, for the most part, of secondary occurrence, even when of a spindle-cell type.

Cancer is very rare in this membrane, and is always secondary. Most of the so-called cancers of the pericardium are *sarcomata* or *lympho-sarcomata.*

Tubercle has been already referred to under Tubercular Pericarditis.

Hydatids of the pericardium are occasionally, but seldom, met with.

HYDROPERICARDIUM.

(See Chapters on Dropsy).

PNEUMOPERICARDIUM (πνεῦμα, *any æriform fluid*).

475. It seems extremely doubtful if air or gas ever accumulates in the pericardial sac independently of some collateral disease or injury of the membrane. Gas is frequently found in the pericardial sac after death; so is it often present in the cavities of the heart. In a large proportion of such instances of pneumo-pericardium the gas has been of *post-mortem* development.

There cannot be the slightest doubt, however, that gas or air has been diagnosed within the sac during life, and that the diagnosis has been verified, as in Begbie's case (No. 171), at the autopsy.

Where the pericardium communicates directly with an air passage, the **gas** is of course atmospheric air more or less altered; but where the gas has been conveyed through a communication established between a neighbouring hollow viscus, such as the stomach, and the sac, or where it is evolved from decomposed effusion within the sac, the gas varies in composition. It will be found that probably the commonest cause is the last of the above mentioned, namely, decomposition of the materials poured out during pericarditis. Several instances of **fistulous communication** between the sac and neighbouring organs, have, however, been put on record by Graves, M'Dowel, Chambers, Tütel, and Saexinger. The pericardium has also been frequently wounded, either traumatically or during surgical operation, and air allowed to enter. According to Walshe (No. 281, p. 627), such traumatic perforation always excites pericarditis.

Punctiform hæmorrhages, into the pericardial membrane, are extremely common in blood diseases such as *pernicious anæmia, scorbutus,* or *purpura hæmorrhagica.* Their causation is not exactly known.

Milk Spots.

476. This name is given to certain thickened opaque patches on the serous layer of the pericardium, of frequent occurrence, and usually associated with enlargement of the heart. As a rule, they are oval shaped, and have a sharp border and a gray colour. They are slightly raised above the surface, and, when microscopically examined, are found to be due to an increase in the quantity and density of the fibrous tissue of the membrane. They are covered by the pericardial endothelium. Their usual site is on the anterior surface of the right ventricle, or on its posterior aspect towards the base. Those at the apex sometimes have an œdematous villus-like aspect, almost as if they had been drawn out by the action of the heart.

They cannot be regarded as an indication of pericarditis, but rather simply as evidence of the effect of friction of an enlarged heart against neighbouring parts. They are evidently due to the same cause as that inducing the pressure marks seen so often on the liver capsule over the gall bladder.

Literature on Diseases of Pericardium.—Consult the various Treatises mentioned under General Literature. **Broadbent** (Great Thickening): Brit. Med. J., 1881, ii. p. 745; (Sarcoma) Trans. Path. Soc., xxxiii. 1881-2, p. 78. **Mathieu** (Tubercular): Arch. gén. de méd., 1883, i. p. 264. **Rousseau:** Essai sur la péricardite tuberculeuse, Par., 1882. **Sibson:** Reynolds' Syst. Med., iv. 1877, p. 186. **Wilson** (Micro-bacillus): Edin. Med. J., xxxi. 1885-6, p. 924.

CHAPTER XXXVI

THE HEART—(*Continued*)

Functional Diseases

477. **Definition.**—By such are meant, *abnormalities in the heart's action unaccompanied by any perceptible organic lesion sufficient to account for them.* They may quite properly be regarded as symptoms of disease rather than as diseases in themselves.

Nerve Supply of the Heart.

478. The heart may be said to derive its nerve supply from three sources—firstly, from the **ganglia** contained within it, secondly, from the **pneumogastric**, and thirdly, from the **sympathetic**.

GENERAL ARRANGEMENT OF THE SYMPATHETIC.

479. **Ganglionic Groups.**—It will be remembered that the ganglia of the sympathetic are located in several groups. The most prominent are the ganglionated cords which run, one on each side of the spinal column, and which are known as the **lateral chains.** Occupying a position in front of the vertebral column there are other ganglia, such as the semilunar and inferior mesenteric, which may accordingly be named the **prevertebral** or **collateral ganglia** (Gaskell). Connected with the viscera themselves, is still another set of ganglia, which, from their position, may appropriately be designated **terminal ganglia**.

Rami communicantes.—From the spinal nerves, branches are given off to the lateral chain of ganglia, and as these establish the communication between the sympathetic and cerebro-spinal systems, they have been named the *rami communicantes.*

Since it is now known that the sympathetic is, morphologically, simply a spinal nerve, the spinal nerves are described as compounded

of three elements—the *posterior root*, the *anterior root*, and the *visceral* or *sympathetic root*. The importance of regarding the sympathetic as essentially a spinal nerve, cannot be over-estimated from a pathological point of view.

These rami communicantes (in the dog, at least, whose nerve distribution closely resembles that of Man), throughout the cervico-cranial, thoracic, and lumbo-sacral regions, contain both medullated and non-medullated fibres (Bidder and Volkmann), while in the region immediately above the thorax, the ramus communicans is devoid of the former (Gaskell, No. 179, vii. p. 10). It would indeed seem that opposite the great outlets of the sympathetic to the main thoracic and abdominal viscera, the rami communicantes are in great part composed of medullated fibres.

In the **thoracic region,** those fibres of the rami communicantes which are not medullated, are according to Gaskell few in number, and have a comparatively unimportant distribution. Unlike the white fibres, they follow a centripetal not a centrifugal course. They evidently arise in the lateral chain of ganglia, and running inwards, supply the corresponding spinal nerves, together with the vertebral (Luschke) and spinal membranes.

Rami efferentes.—Gaskell states (*loc. cit.*, p. 15) that the white rami communicantes after passing into the lateral chain of ganglia, lose their medulla and issue from these ganglia as non-medullated fibres. He regards one of the functions of the lateral chains of ganglia as being that of effecting this conversion of medullated into non-medullated fibres (*loc. cit.*, p. 33). As a rule, they then join the prevertebral or collateral ganglia, and have been designated (Milne-Edwards quoted by Gaskell, *loc. cit.*, p. 3) rami efferentes.

The branches issuing from the collateral ganglia are next distributed to the various organs.

BRANCHES OF SYMPATHETIC TO HEART.

480. In the **cervical region,** the ganglia of the lateral chain are not distributed metamerically, but several seem to have fused together, so that only three are now to be found. They are of large size, and are known as the superior, middle, and inferior cervical ganglia.

The **superior cervical ganglion** lies behind the internal carotid artery, about the level of the second and third cervical vertebræ. In some cases, it is much longer than in others, and may reach down to the level of the fifth cervical.

The **middle cervical ganglion** may sometimes be absent, or may be represented by two smaller ganglia. It lies about the region of the sixth cervical vertebra.

The **inferior cervical ganglion** is of irregular shape, and is larger than the middle. It is sometimes known as the *ganglion stellatum*. The first dorsal sympathetic ganglion is united to it either continuously

or through a short double trunk. It is located in the hollow between the transverse process of the last cervical vertebra and the first rib.

The chord uniting the individual ganglia of the lateral chain, after leaving the middle cervical ganglion, splits into two branches before joining the inferior ganglion. The loop thus formed is known as the **ansa** or **annulus Vieussenii**, and embraces the subclavian artery.

The **thoracic ganglia** are from eleven to twelve in number, of which, the first, or that which is united to the lowest cervical, is the longest. Sometimes the second dorsal becomes confluent with the first.

The *cardiac branches of the sympathetic* take origin from the above-mentioned ganglia in the following manner:—They are usually three, sometimes four in number, namely, the superior, the middle or great, the inferior or small, and the deep.

The superior is one of the descending branches of the superior cervical ganglion.

The middle or *nervus cardiacus magnus* is a compound of several roots springing from the middle ganglion, or, where this fails, from the stem of the sympathetic directly.

The inferior or *nervus cardiacus parvus* usually arises from the inferior cervical and first dorsal sympathetic ganglia by several roots.

The branches from the first dorsal are sometimes united in an independent branch, which then goes by the name of the **nervus cardiacus imus** or **quartus**.

BRANCHES OF VAGUS TO THE HEART.

481. These are given off in two sets—the superior and inferior.

The **superior cardiac branches** are two or three in number, and leave the vagus between the superior and inferior laryngeal.

The **inferior cardiac branches** are given off from the vagus shortly after it enters the chest, partly from the inferior laryngeal nerve.

The **depressor** nerve (Ludwig and Cyon), in the rabbit, it will be remembered, usually arises by one branch from the superior laryngeal nerve, by another from the vagus; or, it may happen, that it springs entirely from the former. It accompanies the common carotid artery, and terminates in the cardiac plexus. It has received the above name, because, on stimulation of its central end, the arterial blood-pressure rapidly sinks, owing to dilatation of the abdominal vessels. In Man, one of the superior cardiac branches of the vagus is usually recognised as the corresponding nerve. It may lie within the vagus sheath or be isolated. In some cases it has been found to receive a branch from the superior laryngeal.

CARDIAC PLEXUS.

482. These various offshoots to the heart from the vagus and sympathetic unite in the *cardiac plexus.*

FIG. 187.—SCHEMATIC VIEW OF THE RIGHT LATERAL CORD OF THE SYMPATHETIC AND ITS CONNECTION WITH THE VISCERAL PLEXUSES AND CEREBRO-SPINAL NERVES.

VI., N. Abducens; (*O*) ciliary ganglion; (*M*) second branch of Trigeminus with Ganglion spheno-palatinum; (*C*) Plexus cervicalis; (*Br*) Brachial plexus; (D_6) sixth, (D_{12}) twelfth intercostal nerve; (L_3) third lumbar nerve; (S_1, S_2, S_5) first, third, and fifth sacral nerves; (*Cr*) N. cruralis; (*Cr'*) N. ischiadicus; (*pn*, *pn'*) N. vagus; (*r*) Ramus recurrens vagi; (*c*) upper; (*c'*) middle; (*c''*) lower cervical sympathetic ganglia; (d_1) first; (d_6) sixth dorsal ganglion; (l_1) first lumbar ganglion; (*cg*) Ganglion coccygeum; (*pp*) Plexus pharyngeus; (*pl*) Plexus bronchialis posterior; (*ca*) Plexus cardiacus; (*co*) Plexus coronarius dexter; (*co'*) Plexus coronarius sinister; (*o*) Plexus œsophageus; (*sp*) Nervus splanchnicus major; (+) N. splan. minor; (++) N. splan. tertius; (*so*) Plexus cœliacus or solaris; (*re*) Plexus renalis; (*pn''*) Plexus gastricus anterior from left vagus; (*ms*) Plexus mesentericus superior; (*ao*) Plexus aorticus abdominalis; (*mi*) Plexus mesentericus inferior; (*mi'*) its connection with (*ic*) the Plexus hæmorrhoidalis; (*hy*) Plexus hypogastricus superior; (*pl*) Plexus hypogastricus inferior; (*v*) Plexus vesicalis.

The cardiac plexus consists of a *superficial* and of a *deep expansion*, the former lying in front of the lower concave border of the arch of the aorta, the latter lying superiorly to the foregoing and behind the aortic arch. The branches of the plexus are intimately interwoven, and communicating branches run between the superficial and deep subdivisions of the plexus and the bronchial and tracheal plexuses.

Branches of Plexus to Heart.—These are chiefly direct offshoots to the auricles, and to the right (anterior) and left (posterior) coronary plexuses.

The *right coronary plexus* accompanies the right coronary artery along the auriculo-ventricular groove to its ultimate distribution on the posterior surface of the heart. It is formed by branches contributed both from the superficial and deep expansions of the cardiac plexus.

The *left coronary plexus* is distributed along with the corresponding artery to the left ventricle, and to the posterior aspects of the heart. It takes origin in the left half of the posterior expansion of the cardiac plexus.

GANGLIA AND TERMINAL BRANCHES OF CARDIAC NERVES.

483. The branches of distribution from the nerves composing these plexuses, are associated with numerous **intracardiac ganglia** occupying the longitudinal and auriculo-ventricular grooves. They are small in size, and lie, for the most part, superficially—close beneath the epicardium (Pettigrew). Some of them, however, of minute size, pierce into the myocardium. In the human heart they are usually imbedded in much fat, and hence are difficult to demonstrate. Those which lie in the auriculo-ventricular groove are most numerous in the neighbourhood of the large veins of the organ.

Schklarewsky (No. 77, 1872, No. 21) found that, in **birds** and small mammals, there is a **chain of ganglia** which runs in the circumference of the **auricular septum.** In birds, the largest ganglion is placed posteriorly where the auricular septum ring of ganglia meets that of the auriculo-ventricular groove. In the **frog**, there is a large collection of nerve cells within the wall of the sinus venosus known as **Remak's ganglion.** From this two nerve cords issue, which pass along the septum of the auricles towards the front of the heart, where, at the point of junction of the auricular septum with the transverse sulcus, they become associated with a mass of large nerve cells known as **Bidder's ganglion.**

From the ganglia situated in the above localities, numerous branches are afforded to the heart muscle. These apparently break up into a fine plexus from which ultimate branches are distributed to the individual muscular fibres.

According to Pettigrew, the number of nerve fibres given off from the ganglia of the heart in Man is less than in mammals, such as the calf.

Schmiedeberg (quoted by Rutherford) and others suppose that the vagus does not directly communicate with the ganglionic apparatus of the heart, but that there is

an inhibitory nervous arrangement, probably ganglionic in its nature, between the two. This theory is opposed by many physiologists, the current notion being that it enters the muscular fibre without any intermediation.

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AUTOMATISM OF HEART MUSCLE.

484. While it is universally granted, at the present day, that the heart is influenced by the various nerves connected with it, yet there has been a tendency of late, owing to certain new facts which have been brought to light, to refer the rhythmic contraction actually back to the muscular fibre itself. F. Franck, for instance (No. 264, p. 253), concludes that the ganglionic influence of the heart is not indispen-

for the production of the rhythmic movements of the organ, which appear to be inherent in the muscular fibre itself.

An experiment, which in former times lent much support to the view that the rhythm was dependent upon the intracardiac ganglia, was that of the **amputation of the heart's apex** in the frog. The heart's apex in the frog is generally held to be free from nerve ganglia, and when it is separated from the rest of the heart it ceases to beat.

It can also be *physiologically* separated by applying a ligature several millimètres below the auriculo-ventricular groove, or by squeezing this region with a pair of fine forceps. The apex will often not begin to beat spontaneously for something like an hour afterwards.

Bowditch's Discovery.—Bowditch (No. 283, 1871, p. 682), however, discovered that if such an apex be supplied with blood-serum containing delphinin, it almost immediately begins to resume its rhythmical contractions. Since this discovery, it has been found that several other means are sufficient to re-excite it.

Thus Merunowicz (No. 283, 1875, p. 252) showed, that, if mammalian blood mixed with indifferent (0·75 per cent) salt solution (1 to 4), be allowed to permeate the organ, the physiologically amputated apex will contract, and when the contractions have once been started, that they can be maintained for some time with 0·6 per cent salt solution alone.

He concluded, *that the heart's apex possessed automatic properties inherent within itself;* and in this view he was supported by V. Basch, Ludwig and Luchsinger, and Aubert. Whether it was the *chemical irritation* (Biedermann and Löwit) of the fluid which brought it about, or whether it was due to the pressure of the liquid within the ventricle (Foster and Gaskell), was for long, and is still, doubtful.

Langendorff (No. 51, 1884, *Phys. Ab. Supplement. Bd.*, p. 56) considers that there is no real automatism inherent in the muscle, but a mere pseudo-automatism occasioned by two causes, namely, (1) mere mechanical irritation, and (2) the chemically irritative effects of the fluid, under which category he includes the nutritive changes produced by it upon the heart's muscle.

Gaskell's Results.—Gaskell's paper on the action of alkalies and acids upon the tonicity of the heart struck a new chord in the solution of the problem of its automatic action. He showed (No. 179, iii. p. 48) that dilute alkalies induce a tonic or constrictive effect upon the muscle of the heart and arteries, while dilute acid (lactic) solutions cause a relaxation or atony; and as all tissues are naturally bathed in the alkaline lymph, it seemed to him that this **alkalinity** was essential for the fulfilment of the heart's so-called automatism.

In a later paper (No. 179, iv. p. 43), he showed that the muscular fibre of the ventricle in the tortoise, which is supposed, equally with that of the frog's apex, to be destitute of nerve supply, possesses, in itself, the property of rhythmically contracting. If separated, it beats rhythmically, and if a strip detached from it be hung up in a moist chamber, it is found to commence beating rhythmically after from three to four hours, and has been seen to go on beating for over thirty hours from the time of its being suspended. The incidence of the contraction is hastened, and is rendered more vigorous, by passing a single induction shock through the strip.

That the rhythm is actually myogonic in its source, that is to say, that it is not dependent upon any possible nerve supply of the part, but is a property inherent in the muscle itself, appears to be favoured by the fact that the strip can be subdivided into fragments which still retain the power of independent rhythm.

It must be borne in mind, however, that these facts are the result of experiments made on the heart of the tortoise alone, and it would be rash to argue that a similar independent automatism prevails in the muscular fibre of mammals and of Man. The experiments are, however, sufficiently remarkable to indicate that certain functional irregularities in the contraction of the heart of Man, might, in reality, be due to causes inherent in the muscular fibre itself. These might be bound up with its nutrition, not necessarily with a disordered state of its nerve supply. The fact that the heart does not cease to beat in an animal when poisoned with woorara, shows that its contractions must be largely independent of nerve stimulus.

It would, thus, almost appear as if the intracardiac ganglia and the extracardiac nerves were **accessories**, and as if the power of rhythmic contraction were, in reality, intrinsic in the muscular fibre itself. It seems doubtful, however, to say the least of it, whether the rhythm in a normally acting mammalian heart is entirely due to this cause.

Sée remarks (No. 284, p. 415) that, in all probability, the ganglia act as accumulators of motor energy, veritable condensers of nerve influx; and that they occasion the discharges by which abrupt and energetic contractions of the organ are elicited.

INFLUENCE OF CARDIAC NERVES ON THE HEART'S METABOLISM.

485. Ransom (No. 179, v. p. 337) presumed that there might be inhibitory fibres in the vagus which tend to induce *constructive metabolic changes* in the heart muscle, while, in the sympathetic, similarly, there might be fibres which cause a *destructive metabolism.*

Gaskell (No. 179, vii. p. 1) regards the condition of equilibrium of muscle denoted by the term *rest* as being brought about by the counterbalancing of the two opposite processes of *destructive* and *constructive metabolism*, called by Hering the acts of *assimilation* and *dissimilation.* Metabolism, he holds, in fact, includes the two opposite processes of destruction and construction, or **katabolism** and **anabolism**. As destructive changes occur when a muscle is set in activity by stimulation of its motor nerve or otherwise, he, accordingly, terms the *sympathetic*, the **katabolic nerve** of the heart. The *inhibitory nerves* of the heart, however, he regards as causing a constructive and not a destructive metabolism, and hence he calls them (vagus) the **anabolic** or trophic cardiac nerves. The action of the one set of nerves is to induce increased activity followed by exhaustion; of the other, diminished activity followed by repair of function.

Paget (No. 149, May 28, 1857; No. 185, xv. 1857, p. 79) entertained something of the same view of the heart's innervation and nutrition, only he regarded the heart's ganglia as presiding over its metabolic interchanges. He believed that the motion of the heart was "an issue of *rhythmic nutrition*, *i.e.* of a method of nutrition in which the acting parts are at certain periods raised, with time-regulated progress, to a state of instability of composition, from which they then decline, and in their decline may change their shape and move with a definite velocity, or (as nervous

centres) may discharge nerve force." In the vertebrate, it is the time-regulated discharge from the heart's ganglia which excites the muscular fibres to contraction; in the invertebrate, this property is inherent in the muscular fibre itself.

Literature on General Physiology of Circulatory System.—As the following references relate chiefly to the more recent works on physiology bearing upon the pathology of the heart, the reader is referred for fuller information to the text-books of Carpenter edited by Power, Foster, M'Kendrick, and Landois translated by Stirling. **v. Bezold:** Untersuchungen üb. d. Innervation d. Herzens, 1863. **Bowditch** (Automatic Contraction of Apex Cordis): Journal of Physiology, i. p. 104; Bericht. d. k. sächsischen Gesellsch. d. Wissensch. Math.-phys. Cl., 1871, p. 682. **Brücke** (Closure of Semilunar Valves on Coronary Arteries): Sitzungsb. d. k. Akad. Wien, Math.-naturw. Cl., xiv. 1854, p. 345; Der Verschluss d. Kransschlagadern, 1855. **Brunton** (Rhythmic Contraction Capillaries in Man): J. Physiol., v. 1884-5, p. 14. **Brunton and Cash** (Electrical Stimulation of Frog's Heart): Proc. Roy. Soc., xxxv. 1883, p. 455. **Danthony:** Contribution à l'étude de la tension artérielle dans les affections cardiaques, 1881. **Dogiel** (Influence of Music on Circulation): Arch. f. Physiol., 1880, p. 416. **D'Espine** (Essay on Clinical Cardiography): Trans. Internat. Med. Cong., 1881, ii. p. 148. **Foster** (Special Case of Inhibition): Pflüger's Arch., v. p. 91; Text-book of Physiology. **Gaskell** (Tonicity): J. Physiol., iii. 1880-2, p. 48; *also* (Structure, Distribution, and Function of Heart Nerves), *Ibid.*, vii. p. 1; *also* (Heart of Tortoise), *Ibid.*, iii. p. 369, iv. p. 43; *also* (Rhythm of Heart of Frog), Phil. Trans. Lond., clxxiii. 1883, p. 993. **Goltz and Gaule** (Influence of Respiration on Circulation): Arch. f. d. ges. Phys., xvii. 1878, p. 100. **Goltz** (Vagus and Heart): Arch. f. path. Anat., xxvi. 1863, p. 1. **Gréhant and Quinquad** (Amount of Pressure necessary to rupture Vessels): Compt. rend. Acad. d. sc. C., 1885, p. 648; (same in Lateral Rupture of Arteries) *Ibid.*, p. 203. **Hoffa and Ludwig** (Cardiograph): Ztschr. f. rat. Med., ix. 1850, p. 102. **Howell and Donaldson** (Amount of Blood Discharged by Left Ventricle): Proc. Roy. Soc., xxxv. 1883, p. 271; *also*, Phil. Trans. Lond., clxxv. 1884, p. 139. **de Jager** (Influence of Sudden Insuff. of Aortic Valve upon Arterial Pressure): Arch. f. d. ges. Phys., xxxi. 1883, p. 215. **Klemensiewicz:** Experimentelle Beiträge zur Kentniss d. norm. u. path. Blutstromes 1886; repr. fr. Sitzungsb. d. k. Akad. d. Wissensch. Mathnaturw. Cl., Wien, xciv., iii. Ab., 1886, p. 17. **Landois:** Grapische Unters. üb. d. Herzschlag, 1866; Text-book of Physiology, trans. by Stirling. **Langendorff** (Rhythm and Automatism of Frog's Heart): Arch. f. Physiol., 1884, suppl. p. 1. **Löwit** (Examination of Circulation in Warm-blooded Animals): Arch. f. exper. Path. u. Pharmakol., xxiii. 1887, p. 1. **Ludwig and Dogiel** (Rapidity of Flow of Blood): Arb. a. d. physiol. Anst. z. Leipzig, 1867, p. 196. **Magini:** (Pressure of Blood in Cavities of Heart): Arch. ital. de biol., viii. 1887, p. 125. **Marey:** Physiologie médicale de la Circulation du Sang., 1863; *also* (Cardiograph) Du mouvem. dans les fonct. de la vie, Paris, 1868, p. 139. **Marey and Chauveau** (Cardiograph): Mém. de l'Acad. de méd., xviii. 1863. **Martin** (Experiments on Suction Pump Action of Heart): Johns Hopkins Univ., Stud. biol. lab., Balt., iv. 1887, p. 37. **Natanson** (on Blood-pressure within the Capillaries after Ligature in mass): Arch. f. d. ges. Physiol., xxxix. 1886, p. 386. **Neumann** (Action of Galvanic Current on the Frog's and on the Mammalian Heart): Arch. f. d. ges. Physiol., xxxix. 1886, p. 403. **Pohl-Pincus** (Trophic Action of Heart Stimuli): Arch. f. Physiol., 1883, p. 261. **Post** (Negative Pulse of Veins): Med. Rec. N. Y., xxiii. 1883, p. 170. **Rutherford** (Innervation): Journ. Anat. and Phys., iii. 1869, p. 402. **Sée:** Recherch. sur l'anatomie et la physiologie du cœur, etc., 1883. **Sewall and Steiner** (Study of Action of Depressor Nerve): J. Physiol., vi. 1885, p. 162. **Sewall and Donaldson** (Intracardiac Pressure and Inhibition through Vagus): J. Physiol., iii. p. 357. **Taljanzeff** (Inhibitory Action of Vagus): Arch. f. Anat. u. Physiol., Physiol. Ab., 1886, Suppl. Bd., p. 31. **Tarchanoff** (Voluntary Acceleration of Heart's Beat): Arch. f. d. ges. Physiol., xxxv. 1884, p. 109. **Thompson** (Photography of Heart in Motion): Med. Rec. N. Y., xxix. 1886, p. 300. **Valentin:** Versuch. einer Physiolog.-path. d. Herzens u. d. Blutgefässe, 1866. **Volkmann:** Die Hämodynamik, 1850. **Webster** (Production of second Heart Sound): J. Physiol., iii. 1880-82, p. 294.

Conditions of Accelerated Beat of the Heart.

PALPITATION.

486. **Vital Phenomena.**—Of all functional disorders this is the commonest, and is more often perhaps an evidence of a purely functional derangement than of organic disease, although it is sometimes associated with the latter.

The heart's action is rapid and tumultuous, and the apex shock seems more widely spread, more diffused, than usual. The excited action is commonly of a paroxysmal character, coming on after muscular exertion, or induced by mental emotion. It is particularly a symptom of **anæmia,** more especially the **chlorotic anæmia** of young girls. It is even more pronounced in Graves' or Basedow's disease (exophthalmic goitre); and it is associated with many other collateral conditions such as indigestion, immoderate use of tea and tobacco, and sexual excesses. Hence it is impossible to elicit any one pathology which will explain all cases.

Physiological Acceleration.—The rapidity of the heart's beat may be temporarily influenced by many minor causes. Thus it is increased by taking nourishment, and is decreased by hunger. Cold (such as the cold-bath) causes a slowing, while warmth augments it. The difference in the frequency of the beat, when the individual is in the prone and in the erect positions is considerable, and is greater in the latter. Muscular exertion increases it, and so does increased rapidity of respiration. In such cases, however, the impulse may not necessarily be increased in vigour, nor has it the diffused character of a palpitating heart.

487. **Acceleration and Work.**—It must not be supposed, however, because a heart beats rapidly, that it necessarily performs more work. This fallacy has been effectually exposed by Vierordt and Marey. A heart beating slowly but energetically, will perform more work than one in which the systoles follow each other rapidly, but in which they are less vigorous.

INFLUENCE OF THE INHIBITORY AND ACCELERATORY NERVES IN THE PRODUCTION OF PALPITATION.

488. In the natural state, the **vagus** seems to be constantly active. It is the great regulating nerve of the heart, tending, as it does, to put a drag upon its action in conditions of irregularity caused by altered tension in the walls of the systemic arteries. It is questionable whether the **accelerator nerves** are also constantly in full play. It seems more likely that their influence is exerted only on occasion, and that their assistance is less frequently required in regulating the heart than that of the pneumogastrics.

Ludwig believes that the only branches of the sympathetic which induce acceleration of the heart's beat, are those from the lower cervical ganglion. Rutherford (No. 5, iii. 1869, p. 402) is of a like opinion.

If the cord be divided immediately below the medulla oblongata and stimulated electrically, the heart's movements are quickened (Wilson Philip, Ludwig, Thiry, and v. Bezold), a result quite in keeping with what we know of the spinal origin of the accelerator or sympathetic fibres.

The action of the accelerators is called forth by strong currents (Boem, No. 104, iv. 1875, p. 255), and it differs from that of the pneumogastrics in not being readily exhausted.

It might be supposed that one cause of palpitation would most likely be found in unduly great stimulation of the accelerators. It is doubtful, however, whether their influence could ever rise to this pitch if the vagus remained unimpaired. In health, the power of the vagus preponderates over that of the sympathetic so much, that, if the floor of the fourth ventricle be stimulated while the vagi are intact, their power of inhibition entirely neutralises the acceleration of the heart's beat, which ought to follow as a consequence. It is only when the vagi are divided, that stimulation of the fourth ventricle calls forth the accelerating effects of the sympathetic (G. Sée, No. 284, p. 240; see also Baxt, No. 286, 1875). The possibility of a protracted acceleration of the heart's beat taking place through the medium of the sympathetic, while the vagi are intact, appears, therefore, to be doubtful.

The only facts that would appear to oppose this conclusion are those derived from the cases of individuals who have been shown to have the acceleration of the pulse under their voluntary control. Tuke (No. 287) mentions a case where an individual was able at will to accelerate his heart beat by ten to twenty in the minute; while Tarchanoff (No. 169, xxxv. 1885, p. 109) gives full details, with experimental investigation, of the case of a student who had the power of accelerating his heart's action thirty-five beats in the minute, and explains the case, not on the grounds of a deficiency in the controlling power of the vagus, but rather on those of increased control over the accelerators. He supposes that this comes to pass by the accelerating centres in the cord being connected with a will centre higher up.

ACCELERATION OF BEAT IN UPRIGHT POSITION.

489. The pulse beats more rapidly (nine to twelve beats difference) when the individual is in the upright position than when reclining. The explanation given by Marey (No. 346, p. 341) is, that the vertical position is favourable, through gravity, to the impelling of the arterial blood onwards in most parts of the body. In the recumbent position, the weight of the column of blood has to be driven onwards by the unaided contractile powers of the heart and arteries; hence there is more resistance and *the arterial pressure rises.* The heart, consequently,

on the principles elsewhere enunciated (Sect. 492), beats less frequently.

PALPITATION FROM UNDULY GREAT MUSCULAR EXERTION.

490. Ludwig and Luchsinger (No. 169, xxv. p. 211) discovered that when the intracardiac pressure in the frog is increased, the cardio-inhibitory influence of the vagus is weakened and may be completely annulled. Sewall and Donaldson (No. 179, iii. p. 357) found the same in the water tortoise (*Pseudemys rugosa*) and large sized bull-frog, and state that the pressure requisite to weaken the inhibitory action of the vagus need not be greater than one to two cm. blood, a pressure which comes within physiological limits. They further concluded "that the mechanism through which variation of pressure within the heart can affect the action of the vagus nerve upon that organ lies largely, if not wholly, within the venous sinus." That is to say, that it is through the venous side of the heart that an increased intracardiac pressure becomes effectual in lowering the influence of the vagus.

Lustchinsky (quoted by above authors) found that the vagus is similarly affected in the dog by raising the intracardiac pressure.

The explanation of the phenomenon is, probably, that the accumulated blood within the heart puts the walls of the sinus and auricles upon the stretch. It is well known that internal pressure excites the heart to motion, and, in the present case, this probably rises superior to the retarding action of the vagus.

These facts may go far to explain the above form of palpitation. When the systemic muscles are unduly exercised, more blood is driven out of them, and is conveyed up to the right side of the heart. It thus causes cardiac distension, and the resulting augmented cardiac pressure on the venous side of the organ, so stimulates it to unduly vigorous effort, that the retarding influence of the vagus is for the time being counteracted. The heart consequently palpitates. Were the heart muscle in an unusually irritable condition, as we may almost presume it is in many forms of palpitation, it would be more readily excited on the individual rising from the prone position, running, climbing a hill, or making other such muscular effort. The cardiac muscle is at once stimulated by the afflux of blood, the vagus is partially or completely inhibited, and the pulsations are consequently increased in number.

PALPITATION FROM VALVULAR LESION OF THE HEART.

491. It seems likely that the distension of the right side of the heart, consequent on the valvular defect, may be one cause of the palpitation here also. Whatever the valvular lesion of the left side

may be, there is a tendency to throw more blood upon the right side, and bring about a distension of its cavities. Such being the case, the heart muscle would be stimulated to excess, and the cardiac beat would be accelerated.

The regurgitant recoil permitted by an incompetent aortic valve will allow of the ventricle being suddenly filled or distended, a condition which is calculated to excite the organ to tumultuous action (see Cohnheim, No. 31, i. p. 49), and which might thus constitute another reason for it palpitating.

The lowering of pressure in the arterial system might explain still other cases (see Sect. 492).

PALPITATION FROM ANÆMIA.

492. In the majority of constitutionally anæmic individuals the heart palpitates without there being evidence to show that the cavities are over-distended. There is none of the venous turgescence of a person suffering from the effects of sudden physical exertion, nor of one afflicted with valvular disease. The whole appearance of the individual would point to the pressure within the heart and vessels being abnormally low. The tendency to syncope, which is so pronounced a symptom in advanced anæmia, would favour this notion.[1] How are these cases to be explained?

It has been shown by Marey (No. 346, p. 338) that the arterial pressure and the rapidity of the heart's beat stand in inverse ratio to each other—the greater the arterial pressure, the slower the cardiac pulsation.

The state of the arterial pressure throughout the body is rapidly communicated to the medulla oblongata, and causes retardation or acceleration of the heart's beat according as it is high or low. When the pressure within the arteries is low, the heart pulsations increase in frequency because the vagus centre is not being excited, and allows the heart, either through its own inherent properties, or through the accelerator nerves, to beat more rapidly. When the pressure within the arteries is high, on the other hand, the vagus inhibitory centre becomes stimulated, with the result that the rapidity of the heart's beat is restrained. This does not follow when the vagi are divided.

The action of **nitrite of amyl** demonstrates very much the same phenomena. It causes arterial and capillary dilatation followed by a lowering of arterial pressure, while the heart beats with increased frequency. It is probable that the increased heart's beat is occasioned by the condition of arterial relaxation being communicated to the vagus centre, for when the vagi are divided and a galvanic current is applied to restore a normal pulse rate, amyl inhalation will not thereafter quicken it (Filehne, quoted by Phillips, No. 296, p. 935).

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[1] It should be added, however, that although the arterial pressure may be low in many anæmics, it is not always so. Broadbent (No. 6, 1882, ii. p. 355) and Sansom (No. 295, p. 67) both state that it is often high.

The above explanation of the palpitation of anæmia might also account for the rapid pulse of **fever,** in which the pressure is said to sink abnormally low.

PALPITATION FROM A DISORDERED STATE OF THE DIGESTIVE ORGANS.

493. This is a common cause of temporary palpitation, and probably its pathology is not in all instances alike. The general supposition is that the loaded abdominal viscera press on the heart and mechanically interfere with its free motion. This explanation will not account for all cases. Reflex inhibition of the vagus by stimulation of its peripheral branches is a much more likely cause.

It is even possible that still another interpretation may, in some cases, be put upon this variety of palpitation. When the functions of the stomach and intestine are not properly fulfilled certain bye-products —**ptomaines**—are generated in the intestine, which, when absorbed, have been shown to act as violent poisons (see vol. ii., "Ptomaines").

It is quite likely that some of these influence the heart muscle directly or through its nerve supply. The various abnormal constituents of the blood, met with in some diatheses, such as that of gout, may act in a like manner.

PALPITATION FROM THE USE OF TOBACCO AND TEA.

494. Persons who are excessive smokers frequently suffer from palpitation, probably the direct effect of the drug. **Nicotin,** when employed experimentally in animals, is found to cause a depression of the pulse rate, followed in course of time by acceleration. The terminal branches of the vagus evidently become paralysed, and the acceleration is thus explained.

The effects of tobacco smoking seem to vary in different individuals. In some, more particularly in young smokers, it causes sudden slowing of the pulse, while in those who are habituated to its use, the effect is usually to accelerate it.

The immediate result of **tea** drinking is to increase the rapidity of the heart's beat. In habitual tea drinkers, palpitation is common. In many such cases, it may probably be explained, not by its direct action on the heart or its nerves, but by its interference with digestion.

PALPITATION FROM OTHER CAUSES.

It would be impossible to enter, at present, into the pathology of all the proximate causes of palpitation. The before-mentioned examples are among the commonest, and many other so-called causes can be ultimately reduced to one or other of these forms. In many instances, the immediate exciting agent seems to be collateral anæmia.

CAUSE OF THE INCREASED IMPULSE AND DIFFUSED APEX BEAT.

495. The increased impulse imparted to the apex beat in most palpitations is evidently due to the spasmodic manner in which the fibre contracts. The diffusion of the beat may be due to a greater extent of surface of the right ventricle coming in contact with the chest wall. Pettigrew (No. 78, p. 242) explains the tilting forwards, and rotation on its long axis, of the normal heart by the special manner of distribution of the muscular fibres, and by the anterior fibres being longer than the posterior. Were these long anterior fibres to contract spasmodically an increased surface would be brought to impinge against the chest, hence diffusing the beat.

Where the right ventricle is dilated, it tends, moreover, to occupy a relatively greater extent of the anterior aspect of the organ, and, for this reason, more of its surface might actually be rendered palpable.

CONDITIONS OF RETARDED BEAT OF THE HEART.

496. The heart sometimes beats with unusual slowness. Taking the normal pulse as between 70 and 75 per minute in Man, it may sink to 40, 20, or even lower.

The inhibition of the heart, in certain individuals, has been found to be under voluntary control. The case of Lieutenant Townsend is often quoted in connection with this subject. He had the power, at will, of arresting both heart beat and respirations, and would lie in a trance, as if dead. His body began to cool and became stiff, the eyes stood immovable, and, finally, he became unconscious. In a few hours afterwards he recovered.

The same explanation no doubt holds good of this as of those cases of voluntary acceleration of the heart's beat, namely, that the vagus centre (in this case) happens to be more intimately connected than usual with a will centre situated higher up.

It is probable, on comparison with the lower animals, that, in Man, cardiac arrest may be brought about reflexly by a variety of means.

Rutherford (No. 294, xxvi. 1869-70, p. 107) has shown that the inhibitory action of the vagus may be excited in warm-blooded animals by stimulation of the central end of the depressor nerve; of the central end of the vagus of the opposite side; of almost any sensory nerve; and, in the frog, of the abdominal viscera, or of the splanchnic and cervical sympathetic.

The application of ammonia vapour to the nose of the rabbit, and the tapping of the abdomen in the frog (Goltz's "Klopf Versuch"), serve to inhibit the heart's beat.

M'William (No. 285, Dec. 13, 1884, p. 19; No. 179, vi. p. 233) demonstrated that the eel's heart can be reflexly inhibited by stimulation of the parietal peritoneum, of the central end of the vagus as it passes along the œsophagus, of the gill apertures; and of the mucous membrane of the mouth and pharynx, of the gills, of the fifth branchial arch; or of the branchial nerves.

In the case of mammals, he also found (No. 149, xliv. 1888, p. 208) that when the cardio-inhibitory centre is inactive, section of the vagi causes no appreciable change in the heart's action. On the other hand, section of the nerves, when the controlling influence of the medullary centre is in full activity, is followed by an increase not only in the rate of the cardiac beat, but also in the contractile force of both auricles and ventricles.

The vagus, he states, seems to exert a direct influence on the muscle of the auricle itself, and appears to inhibit the spontaneous rhythmic tendency inherent in the ventricles.

Conditions of Irregularity in the Heart's Beat.

497. The time occupied in the fulfilment of the various parts of the cardiac cycle of events may be altered. One event may occupy a longer or shorter time than it ought to do. An alteration in the sounds may be so induced.

One of the sounds may be doubled. According to Hayden (No. 288, p. 163), the first sound is less frequently doubled than the second, but he has annotated twelve cases in which the first sound was at fault. The latter is usually an accompaniment of constricted mitral orifice (Hayden).

According to Rosenstein (No. 206, vi. p. 129), Geigel first attempted to explain this phenomenon by the unequal tension in the pulmonary artery and aorta preventing the synchronous closure of the valves of the two vessels. Balfour (No. 289, p. 121) has adopted this view, and refers to the fact that a stenosed mitral will cause the blood to regurgitate upon the lung, and hence close the pulmonary valve prematurely.

Two successive pulsations, rapidly abutting on one another, are occasionally followed by an equally long pause which separates them from the two following. The condition is known as **couple rhythm** or **pulsus bigeminus** (Traube). Similarly, a **pulsus trigeminus** or **quadrigeminus** may occasionally be noticed according to the sequence of the pause.

The bigeminal cardiac pulse is commonly explained by a full systole being followed by an incomplete diastole, on account of which, a second systole supervenes prematurely, this, in turn, being followed by a full diastole. The same theory would account for the trigeminal and quadrigeminal forms of pulsation, the immature diastole being interposed at corresponding intervals.

Collins (No. 59, 1887, i. p. 1229) supposes that a rhythmic rise and fall in the activity of the medullary cardio-inhibitory centre, akin to the rhythm which we know to exist in connection with the respiratory and vaso-motor centres, may account for the pulsus bigeminus.

Along with these forms of pulsation may be included the **pulsus intercurrens**, in which a series of normal pulsations at regular intervals is followed by an interposed beat.

The **paradoxical** form of pulsation (Kussmaul) is where the heart's

beat varies in quality during inspiration and expiration. During inspiration the pulse becomes weak, to gain strength during expiration.

A high and a low beat may alternate. The condition is known as the **pulsus alternans** (Traube). The muscle apparently has not time to recover itself, so as to impart the full impulse to the second beat.

Intermittent pulsation.—The heart beats normally for six, eight, or more pulsations. There is then a more or less prolonged pause.

It is common in gastric derangements. It is questionable whether the heart is actually arrested in the interval. It is more probable that the beat is so feeble as to be imperceptible.

A case is referred to in Carpenter's *Physiology* (1881, p. 295) in which the heart's rhythm intermitted for four to six beats. Its stoppage was accompanied by intense suffering.

The intermission is usually followed by a powerful pulse wave, because the arteries have had time to relieve themselves from any distension, and the blood impelled into them, in their half empty state, renders their expansion all the more apparent.

Cardiac Asthenia.

498. Under the term "weakened condition of the heart" Stokes drew attention to a very serious form of functional derangement. The phenomena of most importance connected with it are an extremely weak, almost imperceptible, apex beat, a quick (108 or more in a minute) and feeble pulse liable to exacerbations, attacks of cardiac asthma, tendency to syncope, and, occasionally, angina pectoris. The radial pulse sometimes has the bigeminal character.

The disease is almost always associated with dilatation of the left ventricle and increase in the size of the heart, but with no other apparent cardiac lesion.

It is a particularly dangerous disease in corpulent individuals, and in a corpulent woman who becomes pregnant, it frequently proves fatal.

Cardiodynia.

499. **Cardiac neuralgia** is common enough as a temporary affection. A special variety of cardiodynia is what is known as **angina** or **angor pectoris**. The disease was first systematically described by Heberden (No. 291, p. 308).

In true angina pectoris, the pain comes on in paroxysms, usually preceded by premonitory symptoms of various kinds. The pain or anguish is of a peculiarly distressing character, and although it has its head centre in the region of the heart, is rarely confined to it, but tends to radiate along the brachial plexus (left most often—Sturge), and into the neck, or it may extend into the intercostal spaces. The

pain causes spasmodic contraction of various muscles, and imparts an expression to the countenance which has been compared to the appearance of anxiety seen in an animal the subject of experiments on the pneumogastrics. The symptom is often associated with *gout*, and hence was called by Butter **diaphragmatic gout**.

The **pathology** of angina is as yet very unsatisfactorily explained. That the **inflamed human heart**, or, at least, its epicardium, is intensely sensitive, cannot be doubted after witnessing the agony called forth on touching it with a trochar or cannula in the operation of paracentesis pericardii.

Marey (No. 346, p. 37) regards the normal mammalian heart as being insensitive to pain, and quotes Harvey as having touched the heart with the fingers in the case of a son of Lord Montgomery, who suffered from a patent wound of the thoracic wall, received in infancy, without eliciting sensation of any kind in the patient. In cases of *ectopia cordis*, the same fact has been frequently verified. He asserts that sounds, etc., introduced into the heart do not provoke signs of pain in an animal, but when roughly handled disturb its rhythm.

Goltz (No. 13, xxvi. 1863, p. 5), on the contrary, alleged that the frog's heart was sensitive, and that the most impressionable part was the sinus, the sensibility diminishing from this region downwards.

Its sensitive nerves are generally supposed to be the superior cardiac branches of the vagus. There is no evidence to prove that some of the sympathetic cardiac branches may also possess a like function. The peculiarly distressing character of the pain would seem to point to the vagus being implicated in true angina.

Morbid Substrata.—*Ordinary cardialgia* may be simply a temporary neuralgic affection, or it may be concomitant with hysteria, epilepsy, Basedow's disease, or dyspepsia, or an accompaniment of mental derangement. In true *angina pectoris*, however, there is usually some distinct morbid anatomical substratum. The commonest met with are *calcification with occlusion of the coronary arteries, chronic endocarditis with valvular lesion, aneurism of the aorta, pericarditis, dilatation of the heart, and chronic myocarditis.*

It is often asserted that the *cardiac plexus* is at fault. It has been stated to be in a condition of hyperæmia or inflammation. That the cardiac plexus is not the actual seat of the malady, would seem to be borne out by the fact that so little pain frequently accompanies aneurism of the aorta, a disease in which it must be seriously compressed. Disease of the heart muscle, in some form, is, perhaps, the commonest gross abnormality.

Condition of the Arteries.—Brunton (No. 59, 1867, ii. p. 97; No. 5, v. p. 92; and No. 293, iii. p. 191) was led to believe, from the limited apex and other characters in the sphygmographic tracing, taken during the period of the attack of pain, from a man with aortic disease and angina-like spasms, that the arteries were in a state of unduly great tension. He employed nitrite of amyl for relief of the vascular spasm with almost complete success. This spasm of the vessels has been regarded by some (Traube, Nothnagel, etc.) as being in some

way intimately connected with the cause of the disease. A more likely view, however, probably is, that the spasm of the vessels and rise in blood pressure are due to the pain.

In a case which came under the notice of the author some time since, the only lesion was a chronic fibrous myocarditis of the ventricles. The wall of the ventricle was over an inch in thickness, owing to excessive deposit of fibrous tissue. The nerves and muscular fibres were surrounded by the cicatrix-like mass, and were compressed and atrophied from the pressure of its fibres. The explanation which seemed most feasible was, that the pain had been caused by the pressure of the cicatrix upon the cardiac nerve terminations, very much as in the case of a tight cicatrix in a stump.

Literature on Angina Pectoris.—**Balfour**: Edin. Med. J., xxvi. 1880-1, p. 769. **Barr**: Med. Press and Circ., xxxvii. 1884, p. 280. **Gairdner**: Reynolds' Syst. Med., iv. 1877, p. 535. **Gélineau**: Traité de l'angine de Poitrine, 1887. **Hay (M.)**: Practitioner, xxx. 1883, pp. 179, 321. **Huchard**: Rev. de Méd., April, June, Aug., and Sept., 1883. **Putnam**: v. Ziemssen's Cyclop. Pract. Med. Suppl., 1881, p. 604. **Sturge**: Brain, v. 1883, p. 492.

Literature on Functional Diseases of Heart.—**Broadbent**: Brit. Med. J., 1887, i. pp. 655, 707, 763. **Da Costa** (Irritable Heart): Am. J. Med. Sc., 1871. **Feuerbach**: Berl. klin. Wochnschr., xvii. 1880, p. 670. **Fothergill** (Palpitation): Lancet, 1870, ii. p. 179. **Fraenkel** (Weak Heart): Berl. klin. Wochnschr., xvii. 1880, p. 12. **Garland**: Boston M. and S. J., cix. 1883, p. 25. **Hurd**: Med. Rec. N. Y., xxiv. 1883, pp. 422, 537, 699. **Jacob** (Reflex Influence of Baths on Heart): Arch. f. path. Anat., xcvi. 1884, p. 36. **Keyt**: Boston M. and S. J., cix. 1883, p. 30; J. Am. Med. Ass. Chicago, 1883, i. p. 135. **Krishaber**: Gaz. hebd. de méd., ix. 1872, p. 323 *et seq; also*, Dict. encycl. d. sc. méd., xiv. 1873, p. 100. **Lannois**: Rev. de méd., iv. 1884, p. 424. **Myers**: Diseases of the Heart among Soldiers, 1870. **Osler**: Overstrain of the Heart (Bibliography), Montreal, 1878. **Robinson**: Med. Rec. N. Y., xvii. 1880, p. 713. **Rosenbach**: Deut. med. Wochnschr., viii. 1882, p. 157. **Sée**: Maladies du Cœur, 1882; *also*, Gaz. d. hôp., xxxviii. 1865, p. 73; *Ibid.*, p. 77. **Thurston**: Med. Times and Gaz., 1881, i. pp. 454, 484. **Traube**: Ges. Beiträge zur Pathologie, iii.

CHAPTER XXXVII

THE HEART—(*Continued*)

Weights and Measurements of Normal Heart

500. For the last thirteen years the author has kept an accurate record of the size of the apertures, the thickness of the walls, the length of the ventricular cavities, the weight of the organ, etc., in nearly every *cadaver* which has passed under his hands as pathologist to the Edinburgh and Aberdeen Royal Infirmaries. The facts derived therefrom have mainly served as the basis of the following conclusions.

The measurements of the orifices were all made by means of the graduated cones previously described (Sects. 1 and 5).

The size of the ventricles was estimated by measuring the distance *from the apex of the cavity up to the base of the nearest sigmoid cusp.* It is, of course, apparent that this method of ascertaining the size of the ventricle is open to objection. As a matter of experience, however, it will be found that it gives a much more accurate estimate of the total capacity of the cavity than might at first be supposed, and, when combined with a description of its general appearance, must be held to be infinitely preferable to any unsupported statement.

The measurement of the walls was always taken at their thinnest and at their thickest parts. The subpericardial fat was not included, and the parts selected were those intervening between the musculi papillares.

The following figures, of course, represent average measurements.

In estimating the weight and dimensions of any organ, it is necessary to draw conclusions only from healthy individuals who have met their death suddenly from traumatic causes. In no case ought this to be more rigidly adhered to than in that of the heart.[1]

The following statistics were derived from the examination of twenty-seven males and of four females, all over nineteen years of age,

[1] The discrepancies to be found in the figures given by Peacock, Clendinning, Bizot, Rosenstein and others, are doubtless due to failure in the observance of these precautions.

who were in perfect health at the time of death, and who were accidentally killed.

The heart was excised in all cases by cutting through the arch of the aorta at its middle, and through the pulmonary artery close to its bifurcation. The attached parts of the vessels were included in the weights, and the organ was opened and washed out before the weight was ascertained.

The results, briefly stated, show, that the commonest **weight** of the *male* heart was from 12 to 13 oz., and that it ranged between 10 and 16 oz. They also demonstrate that the heaviest organ occurs in the tallest individuals, although there were exceptions to this rule, and that the heart, although generally, was not invariably of low weight in persons of small stature.

In the *female*, the organ usually weighed between 10 and 11 oz. It ranged from 7 to 15½ oz.

The **diameters of the various orifices** were found to be as undernoted in the accompanying table :—

Diams. of Orifices—Male.

	Greatest.	Least.	Average.
Aortic . .	1·3 in.	·9 in.	1 in.
Mitral . .	1·8 „	1·1 „	1·4 „
Pulm. Art. .	1·5 „	1 „	1·2 „
Tricuspid .	2·2 „	1·3 „	1·8 „

Diams. of Orifices—Female.

	Greatest.	Least.	Average.
Aortic . .	1 in.	·8 in.	·9 in.
Mitral . .	1·5 „	1 „	1·2 „
Pulm. Art. .	1·3 „	1 „	1·1 „
Tricuspid .	1·7 „	1·4 „	1·5 „

The taller the subject, the larger the orifices; but there are exceptions to this general statement. When one of the orifices is large the others are usually correspondingly so.

The measurements of the **ventricular cavities,** estimated from the fixed points before mentioned, show that, in the male, the lowest for the *left* ventricle was 2½ in., the highest 3¾ in., and the average 3¼ in.; while, in the female, the lowest was 2¼ in., the highest 3½ in., with an average of 3 in.

That of the *right* ventricle in the male ranged between 3 and 4 in., with an average of 3⅜ in.; while, in the female, it lay between 3 and 3¼ in., with an average of 3 1/16 in.

The **thickness of the left ventricular wall** was, as a rule, found to be about ¼ in. at the apex, and ½ in. at the base, both in the male and female; while the *right* ventricle was on an average ⅛ in., all

over, in both sexes. Parts of it occasionally measured as much as $\frac{1}{4}$ in. or as little as $\frac{1}{16}$ in.

As the following statistics of diseased hearts include both males and females, it will be necessary to frame an **approximate** statement of the weights and measurements for comparison. The following is founded on the different averages just given for both sexes.

TABLE OF AVERAGE WEIGHT AND MEASUREMENTS OF THE NORMAL HEART.

WEIGHT 10 TO 13 OZ.

Diams. of Orifices.		*Cavities and Walls.*	
Aortic	·9 to 1 in.	L. Vent.	3 in. to $3\frac{1}{4}$ in.
Mitral	1·2 ,, 1·4 ,,	Wall	$\frac{1}{4}$ in. (at thinnest) to $\frac{1}{2}$ in. (at thickest)
Pulm. Art.	1·1 ,, 1·2 ,,	R. Vent.	$3\frac{1}{16}$ in. to $3\frac{3}{8}$ in.
Tricuspid	1·5 ,, 1·8 ,,	Wall	$\frac{1}{8}$ in. (all over)

Literature on Weight and Dimensions of Heart in Health and Disease.—**Beneke**: Ueb. d. Volumen d. Herzens u. d. Weite d. Art. pulm. u. Aorta ascend. in d. verschied. Lebensaltern, 1879. **Cammann**: Med. Gaz. N. Y., vi. 1870-1, pp. 169, 183, 281. **Peacock**; Trans. Path. Soc., xiii. 1862, p. 64; *also*, Reynolds' Syst. Med., iv. 1877, p. 3; *also*, Month. J. Med. Sc., 1854. **von Buhl** (Measurement of Vents. and Large Vessels): Mitth. a. d. path. Inst. zu München, Stuttg., 1878, p. 26.

CHAPTER XXXVIII

THE HEART—(*Continued*)

DISEASES OF MYOCARDIUM

FATTY HEART.

501. **Definition.**—Two diseases, to a certain extent antagonistic in their origin, are included under this designation—(1) An infiltration or loading of the heart with fat (*cor adiposum*); and (2) a true fatty degeneration or metamorphosis of the heart muscle.

FATTY INFILTRATION.

The subepicardial fat is much increased in quantity, especially in the auriculo-ventricular furrow. The fat sometimes penetrates into the heart muscle, and is said to occasion an **atrophy** of the fibre. Such a result, however, is rare, if it ever follows. It is more likely, in cases where atrophy of the fibre has been present, that the fat has merely taken the place of the heart tissue, just as sometimes happens in other organs (*e.g.* the kidney).

Cases have been recorded in which the fat has accumulated to such an extent as to interfere with the motion of the organ (Fothergill, Leyden, etc.)

FATTY DEGENERATION.

502. This is a much more important disease, from the fact that it tends to impair the integrity of the heart's contractions.

It may conveniently be considered under three subdivisions: (1) General fatty degeneration where the whole heart, or an entire ventricle, is affected; (2) where the disease is localised to a particular spot of the heart's wall, and where the degeneration is a secondary effect of some pre-existing disease of the organ; and (3) where it is due to poisonous substances.

(1) GENERAL FATTY DEGENERATION.

Naked-eye Appearances.—The heart is usually below the average size, and is undernourished. Its surface, however, is occasionally covered by a somewhat dense layer of epicardial fat. It feels lax and flabby, has a general pale fawn-brown colour, variegated with grayish-yellow striæ in the parts which are the special seat of the degeneration. The coronary arteries are quite pervious, and are usually free from disease.

The parts in which the degeneration is most evident are the *musculi papillares* and *columnæ carneæ*. The left ventricle is more often, and more extensively, fatty than the right, and, frequently, the whole

FIG. 188.—FATTY DEGENERATION OF MUSCULUS PAPILLARIS.

of its musculi papillares and columnæ may be found simultaneously implicated in the degeneration. The appearance they present is quite characteristic.

They may not be much reduced in bulk—at least not disproportionately to the rest of the heart. They generally have the light brown colour of the heart muscle, but, over and above this, present a *striated* or *brindled* appearance from there being wavy pale yellow striæ running across them. The appearance has been compared to that of a thrush's breast, or the fur of a tabby cat. The brown coloured intervals between the yellowish striæ are of equal breadth with the latter, usually about half a line in extent.

When the muscular tissue is incised, it presents an anæmic appearance, the striation which is so evident immediately beneath the endocardium is lost, and a uniform pale yellowish-brown colour takes its place.

The cause of the striation is, that the bands of yellow tint are fatty, while the fibres in the intervening brownish-coloured interval are almost healthy. It is one of the characteristics of this form of fatty degeneration, that the fibres are never universally fatty. What it is that determines their becoming fatty in the regular band-like intervals, above referred to, has not as yet been explained.

Eichorst (No. 323) has shown that, in birds, dogs, and rabbits there are certain branches of the pneumogastric which possess a direct trophic action upon the muscular fibres of the heart, so that when the trunks of the vagi are divided, fatty degeneration follows in the heart muscle within a few days. Whether the partial distribution of the degeneration is due to the areas of expansion of the terminal filaments of these nerves may be open to conjecture.

FIG. 189.—CLOUDY SWELLING. HEART FIBRE (×350 DIAMS.)

Microscopic Appearances.—The earliest change noticeable in the fibre is the *precipitation of finely granular albuminous matter* in the myosin—a cloudy swelling. The fibre increases in dimensions, is more regularly rounded, the striæ become indistinct, and, here and there, a small *oil globule* may be detected. The granularity vanishes on the addition of glacial acetic acid or solution of potash, thus showing that it is of an albuminous nature. Side by side with these fibres may be seen others which are comparatively little altered or quite healthy.

In a stage somewhat more advanced, the oil globules increase in number. They are scattered diffusely through the fibre, and are always more abundant in some parts of its course than in others. They are sometimes aggregated round the muscle nuclei, but the latter do not appear to be the points of departure of the degeneration.

When the degeneration has reached its climax, the fibres assume a black granular appearance. They can be readily distinguished, on this account, with a low magnifying power, from those which as yet have not degenerated; and, with a higher amplification, the globules within them can be seen as clear centred highly refractile bodies, differing a little in size, but not much, if at all, larger than a coloured blood corpuscle. The majority of them are considerably smaller. The globules are held together by the remains of the albumin of the fibre. The whole fibre appears to be enlarged, and resembles, unless in shape,

a compound granular corpuscle. It ultimately disintegrates and allows the globules to escape, its destruction being thus completed.

Causes.—*General anæmia*, more particularly *progressive pernicious anæmia*, is by far the commonest. When an animal is rendered artificially anæmic by venesection, the heart muscle becomes fatty. Hence the relationship of the anæmia to the degeneration is probably simply one of *malnutrition*.

FIG. 190.—FATTY DEGENERATION. HEART FIBRE (×350 DIAMS.)

Effects.—The heart muscle may *suddenly* fail to cope with the blood within it, and thus induce a rapid syncope. What is even more usual, is, that it *gradually* becomes incompetent to carry on the circulation, and the individual dies in a state of asthenia. Whether such a heart, when advanced in the disease, ever recovers, is unknown. If the spanæmia were remedied, it is possible that it might. As before mentioned, there is always a large proportion of the fibres which are unaffected; and it is likely that the place of those destroyed would be quickly filled up by others freshly generated.

This form of fatty heart does not predispose to aneurism of the organ, apparently because the destruction of the fibre, at any given point, is always partial.

For effects upon the pulse tracing, consult Kisch (No. 43, xxi. 1884, p. 132).

(2) *PARTIAL FATTY DEGENERATION.*

503. **Causes.**—The diseases of the heart which precede this are usually such as exert an ischæmic influence upon the part implicated. Thus, of all causes, disease of the coronary arteries is the most potent. The branches of these vessels may be regarded as, in great part, terminal in their distribution, hence when they become atheromatous, calcareous, or thrombotic, the nourishment of the heart suffers locally. A patch of fatty degeneration may sometimes be seen at the tip of a musculus papillaris, underlying an old endocardial thickening; but in chronic general fibrous myocarditis, fatty degeneration of the fibre need not follow, provided that the arterial supply remains unimpaired. In the neighbourhood of an abscess of the heart, the fibre will also be found to be more or less fatty.

General Appearances.—The striation of the heart wall, which is so striking a feature of the foregoing, is usually absent in this. In its place, a patch of muscle, most likely that of a ventricle, is softened, has become extremely friable, sometimes gelatinous in texture, and is

of a pale yellowish-brown colour (*myomalachia cordis*). The degenerated patch sometimes has a greasy feeling, and oil globules may be detected with the naked eye; while, microscopically, the appearances before described are at once evident, the degenerated fibres being more abundant than in the general form.

Although it is more common to find the degeneration localised to *one* spot, yet, in some cases, there may be *several*, corresponding to the number of vessels whose circulation has been interrupted.

Effects.—The diminished resistance of the wall may lead to an *aneurismal bulging* of the endocardium; or a *simple rupture*, with fatal extravasation into the pericardium, may terminate the patient's life.

The degeneration, on the other hand, may be limited to so small an area that no perceptible ulterior influence can be detected.

Quain (No. 34, xxxiii. 1850, p. 153) gives twenty-five in sixty-eight cases as the proportion in which rupture of the heart from fatty degeneration had occurred.

Literature on Myomalachia Cordis.—**Laveran**: Union méd., 1878, xxiii. **Tautain**: De quelques lésions des artères coronaires comme cause d'altération du myocarde. Thèse de Paris, 1878. **Virchow**: Arch. f. path. Anat., iv. 1852, p. 266. **Wagner**: Arch. d. Heilk., i. 1860, p. 185. **Wilks and Moxon**: Lectures on Path. Anat., 1875, p. 122. **Ziegler** (Myomalachia): Arch. f. path. Anat., xc. 1882, p. 211.

(3) *FATTY DEGENERATION FROM POISONOUS SUBSTANCES.*

504. **Phosphorus** has long been notorious as a toxic agent whose effects manifest themselves in fatty degeneration of various organs and tissues, the heart included. **Arsenic** and **antimony** possess similar properties, although they are less harmful.

Wagner (No. 211, p. 305) states that v. Hauff (1861) was the first to show that fatty liver was a frequent coincidence in phosphorous poisoning. Wagner himself (No. 324), Lewin (No. 13, xxi. 1861, p. 506), Klebs (No. 13, xxxiii. 1865, p. 442), Senftleben (No. 13, xxxvi. 1866, p. 520), and many others, have since proved experimentally that the heart suffers fatty degeneration along with other tissues. The whole muscular system seems to be affected by it.

Saikowsky (No. 13, xxxiv. 1865, p. 73), and Grohe and Mosler (*Ibid.*, p. 208), demonstrated that arsenic and antimony have a like effect.

CHEMICAL ANALYSIS.

505. Weber's (No. 13, xii. 1857, p. 326) researches seemed to show that the total amount of fat contained in the organ did not materially differ from that of one in health. This may probably be accounted for by general emaciation having been present in the cases he examined. Boettcher and Valentiner (quoted by Schroetter), on the contrary, found it to be augmented.

FATTY HEART FROM A FORENSIC POINT OF VIEW.

506. It is frequently a matter of extreme importance medico-legally to be able to recognise the fatty heart, or, quite as much so, to be

able to say when a heart is not fatty. When the unequivocal signs of the disease just related are present, there cannot be much doubt on the subject; but, without question, positive evidence of the heart being fatty is often given by unskilled medical witnesses, where the fibre was simply anæmic, or in some of the other semi-morbid conditions which may be so readily mistaken for it.

In forming an opinion in any particular case, the following may be useful as a guide :—

(1) If the macroscopic signs of the disease previously described are not noticeable, the presumption in favour of the heart being fatty is weak. If there has been fatty degeneration of the fibre sufficient to cause death, it will leave some trace of its presence perceptible to the naked eye.

(2) If no macroscopic changes are seen, extreme care ought to be exercised in interpreting those which may be found microscopically.

(3) A pale flabby heart is not necessarily fatty. Fatty degeneration is a comparatively rare disease, while hearts blanched and relaxed from anæmia are of everyday occurrence.

(4) Very obese individuals do not usually suffer from fatty degeneration of the fibre. The heart in them may be loaded with fat, but the fibre is often particularly healthy and well nourished. Obesity is a sign of over-nutrition, fatty degeneration of the heart of under-nutrition. In very anæmic persons with fatty degeneration of the heart, however, there may be a considerable quantity of surface fat.

(5) Microscopically, the degeneration may be confounded with other pathological states of the fibre. These are chiefly **pigmentary deposit** and **cloudy swelling**. The former may readily be distinguished (*a*) by the pigment being granular, not globular; (*b*) by its having a reddish-yellow colour; (*c*) by its being deposited in spindle-shaped masses, through the fibre, at intervals corresponding to the position of the nuclei; (*d*) by its becoming of a dull gray not of a black colour with perosmic acid solution; and by its being brought more prominently into view by the action of glacial acetic acid or solution of potash.

Cloudy swelling of the fibre is common where there has been a feverish state of the body, and in acute rheumatism. It is often, as before mentioned, a precursor of the fatty change. It may, however, be merely of temporary duration and unassociated with fatty disease.

It can be readily detected and differentiated (*a*) by its being a finely granular precipitate, not a globular deposit; (*b*) by its being at once clarified by glacial acetic acid or by solution of potash.

(6) The healthiest heart muscle may have a globule or two of oil adhering to it or lying in its neighbourhood.

Method of procedure in examining the fibre.—(*a*) Examine carefully for naked-eye evidences of the disease.

(*b*) Cut out a thin strip, tease with needles in neutral salt solution or water, and examine with both high and low power.

(*c*) Treat separate portions of it with glacial acetic acid, and with solution of potash. Fatty particles ought to be rendered more prominent by the clarification of the surrounding albumin.

(*d*) Treat fine shreds of fibre by the prolonged application of alcohol followed by sulphuric ether, and notice, on teasing out the fibre, whether the globules have a tendency to dissolve.

(*e*) Steep pieces of the fibre for a night in ½ per cent solution of perosmic acid, and notice whether the globules blacken.

(*f*) Never rely on the examination of anything but the fresh fibre.

Literature on Fatty Heart.—**Begbie (J.)**: Month. J. med. Sc., Mar. 1851. **Coats** (from Single Large Hæmorrhage): Glasg. Med. J., x. 1878, p. 283. **Curschmann**: Deut. Archiv., f. klin. Med., xii. 1874, p. 193. **Fothergill**: Ed. Med. J., xxxii. 1886-7, p. 385. **Fraenkel** (Experimental): Charité-Ann., ii. 1877, p. 309. **Gowers**: Reynolds' Syst. Med., iv. 1877, p. 760. **Grohe and Mosler** (from Arsenic): Arch. f. path. Anat., xxxiv. 1865, p. 208. **Holmes (T.)** (F. H. and administration of Chloroform): Trans. Path. Soc., xv. 1864, p. 69. **Jeullien**: De la dégénérescence graisseuse du cœur dans ses rapports avec le pouls la syncope et les troubles respiratoires, 1875. **Kennedy**: Observations on Fatty Heart, 1880. **Kisch** (Influence on Pulse): Berl. klin. Wochnschr., xxi. 1884, p. 132. **Klebs** (from Phosphorus): Arch. f. path. Anat., xxxiii. 1865, p. 442. **Krylow**: Arch. f. path. Anat., xliv. 1868, p. 477. **Lewin** (from Phosphorus): Arch. f. path. Anat., xxi. 1861, p. 506. **Leyden**: Berl. klin. Wochnschr., xv. 1878, pp. 221, 237; Charité-Ann., iv. 1879, p. 206; Zeitschr. f. klin. Med., v. 1882, p. 1. **Ormerod**: Lond. Med. Gaz., ix. p. 739. **Piotrowski**: Dégenérat. graisseuse du cœur. Thèse de Paris, 1865. **Ponfick**: Berl. klin. Wochnschr., x. 1873, pp. 3, 13. **Quain**: On Fatty Diseases of the Heart, 1851; Lon. Med. Gaz., Mar. 1850; Med. chir. Trans., xxxiii. 1859, p. 121. **Saikowsky** (from Arsenic, Antimony, and Phosphorus): Arch. f. path. Anat., xxxiv. 1875, p. 73. **Senftleben** (from Phosphorus): Arch. f. path. Anat., xxxvi. 1866, p. 520. **Virchow** (Acute in Pericarditis): Arch. f. path. Anat., xiii. 1858, p. 266; (in Chlorosis) Ueb. d. Chlorose, etc., 1872, p. 17. **Wagner**: Die Fettmetamorphose d. Herzfleisches, 1864. **Weber**: Arch. f. path. Anat., xii. 1857, p. 326. **West** (Acute): Trans. Path. Soc., xxxiii. 1881-2, p. 74.

Rupture of the Heart.

507. The possibility of the healthy heart rupturing in Man from overstrain may be doubted. It is said to occur in animals hunted to death. When it does rupture in Man, the fibre will usually be found to be suffering either from fatty degeneration or from abscess.

The blood may escape in a sudden gush, as where the part has been aneurismal previous to its giving way, or it may continue to leak from a small fissure into the pericardial sac for some hours before death. Blood may be effused under the epicardium and find its way over a large surface of the heart previous to the actual rupture taking place.

When a gush of blood suddenly distends the pericardial sac, the heart seems to cease beating almost at once. The individual becomes extremely livid in the face and neck, and expires instantaneously.

Literature on Rupture of Heart.—**Baldwin**: Brit. Med. J., 1884, i. p. 12. **Mackenzie**: Brit. Med. J., 1884, i. p. 309. **Mickle**: Ed. Med. J., xxix. 1883-4, p. 710. **Wyckoff**: Buffalo M. and S. Journ., xxiii. 1883-4, p. 297.

Pigmentary Involution.

508. In nearly all individuals above middle life, the heart fibre

shows a little pigmentary degeneration. The pigment is granular hæmatoidin of a reddish-yellow colour, and is collected in small spindle-shaped heaps around the muscle nuclei. It does not appear to embarrass the functions of the organ, and is without much effect upon the striation of the muscle.

FIG. 191.—PIGMENTARY INVOLUTION. HEART FIBRE (×350 DIAMS.)

In old people, however, the pigmentation is accompanied by a shrinking and involution of the fibre.

The heart, under such circumstances, is below weight; it is hard and tough; the vessels on its surface are frequently tortuous, and the areolar tissue immediately surrounding them œdematous; while the muscular fibre has a dark chocolate or morone colour. The ultimate fibres are of narrow diameter, the striæ remain distinct, and the nuclei are pigmented as above described.

Literature on Atrophy of Heart (Small Heart).—**Bulley:** Med. Times and Gaz., 1872, ii. p. 252. **Church:** Trans. Path. Soc., xix. 1868, p. 147. **Gowers:** Art. in Reynolds' Syst. Med., iv. 1877, p. 687. **Salvioli** (Cyanotic): Arch. per le sc. med. Torino, iii. 1879, No. 6.

WAX-LIKE DISEASE.

509. This is a commoner lesion than is generally supposed. It will be found present in the majority of instances of general wax-like disease, but, on account of its not causing any very distinctive naked-eye abnormality, it is frequently passed over undetected.

The only appearance to indicate its presence is a little milky opacity of the endocardium of one or more of the chambers, usually of an auricle, and, by preference, of the right.

Virchow (No. 13, xi. 1857, p. 188) seems to have first observed the disease, but, since then, Eberth, Heschl, Ziegler, the author, and others have described it in more detail (see Bibliography).

Naked-Eye Characters.—The heart is undernourished and somewhat anæmic, but does not show any indication of being waxy, over and above the opacity of the endocardium already referred to. When iodine solution is applied to the endocardium, numbers of isolated brown spots or patches appear upon it.

Microscopic.—Sections stained in gentian violet show that the above reaction is due to isolated deposits of the wax-like substance lying in the membrane. The chief seat of the infiltration, however, is the myocardium, between whose bundles and individual fibres large and numerous pink stained homogeneous masses can be detected. By compressing the muscular fibres, they cause them to atrophy. The small arteries, as in other waxy organs, are affected at an early period

of the disease. The epicardium and pericardium do not seem to suffer.

Hyaline Degeneration.—Bouchut (No. 325, 1872, No. cxvii. p. 932), Labadie-Lagrave (No. 326), and Rosenbach (No. 13, lxx. 1877, p. 352), describe a peculiar hyaline swelling of the muscular fibre which occurs in the heart during diphtheria. It is similar to that of the body muscles in typhoid. Rosenbach regards it as a form of inflammation. The hyaline substance resulting from the degeneration does not give the waxy reactions.

Literature on Waxy Heart.—**Eberth:** Arch. f. path. Anat., lxxx. 1880, p. 160. **Hamilton:** J. Anat. and Phys., xviii. 1883-4, p. 54. **Heschl:** Wien. med. Wochnschr., xxvi. 1876, p. 25; *Ibid.*, xxvii. 1877, p. 625. **Virchow:** Arch. f. path. Anat., xi. 1857, p. 188. **Ziegler:** Not published, but mentioned in Macalister's transl. of his Lehrbuch d. path. Anat., p. 90.

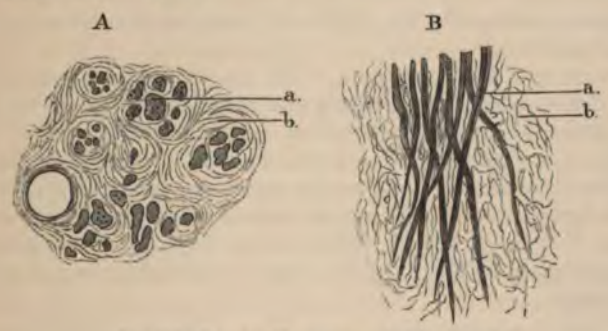

FIG. 192—CHRONIC MYOCARDITIS (×300 DIAMS.)

A, Cross section of the fibres; (*a*) fibres in various stages of atrophic destruction; (*b*) surrounding cicatricial tissue. B, Same seen on horizontal section; (*a*) fibres; (*b*) surrounding cicatricial tissue. (Picro-carmine and Farrants.)

MYOCARDITIS.—(*μῦς, μυός, a muscle*).

510. **Definition.**—An inflammation of the muscular substance of the heart.

General Description.—The disease runs either an acute or a very chronic course.

In the acute form, the inflammation usually ends in abscess, often followed by rupture of the wall. It is frequently pyæmic in its nature, or is an accompaniment of diphtheria, typhoid, anthrax, scarlet fever (Goodhart), etc. The abscesses, when pyæmic, are sometimes multiple.

In the chronic form, the disease may last for years. It appears to be essentially a cirrhosis and results in the substitution of coarse fibrous tissue for the muscular substance of the heart.

The wall of the **left ventricle** is its usual seat. It is almost unknown on the right side. The wall may be over an inch in thick-

ness, or may be so attenuated that it resembles a piece of thin leather. The difference depends on the great or small amount of fibrous tissue which may be deposited within it.

At other times, there are only fibrous cicatrix-like patches of new tissue scattered at intervals through the muscle, and always best seen towards the apex. They are often exclusively localised to this neighbourhood.

The cirrhosed wall is hard and tough, and when of increased thickness, is, in great part, composed of dense gray coloured fibrous tissue with patches of muscle fibre interspersed at intervals throughout it.

The disease is almost always associated with chronic endocarditis or pericarditis, or, just as often, with both combined.

Huber, however (No. 13, lxxxix. 1882, p. 256), disbelieves in the direct connection of the disease with endo- or pericarditis, and traces its causation rather to an arterio-sclerosis of the branches of the coronary arteries.

Microscopic Appearances.—The cicatricial tissue is usually very old and dense, with comparatively few young cells mixed up with it. It closely envelops the bundles of muscular fibres, seeing that it springs from a thickening of their perimysium. It gradually contracts, and causes them to shrink, to become granular, and, finally, to undergo complete atrophy, so that in certain strands of heart wall not a single muscular fibre may be left. *They do not become fatty* as a result of the compression. Their nuclei may occasionally be seen to be proliferating.

Literature on Myocarditis.—**Arnold:** Die Myocarditis, 1866. **Brehme:** Ueb. Myocarditis fibrosa, 1883. **Collat:** Lyon méd., xxxii. 1879, p. 253. **Delafield:** N. York Med. Journ., xxxi. 1880, p. 184. **Dickinson** (Syphilitic): Trans. Path. Soc., xiii. 1861-62, p. 60. **Ferguson:** Med. Rec., N. Y., xxv. 1884, p. 502. **Fuller:** Trans. Path. Soc., xix. 1867-68, p. 108. **Gairdner (W. T.):** Month. M. J. Med. Sc., xix. 1854, p. 79. **Goodhart** (Suppurative): Trans. Path. Soc., xxxi. 1879-80, p. 70. **Greenfield:** Trans. Path. Soc., xxvi. 1874-75, p. 58. **Hilton-Fagge:** Trans. Path. Soc., xxv. 1873-74, p. 64. **Huber:** Arch. f., path. Anat., lxxxix. 1882, p. 236. **Juhel-Rénoy:** Étude sur la sclérose du myocarde, etc., 1882. **Kirchner:** Beiträge zur Lehre v. d. Myocarditis fibrosa, 1884. **Knoll:** Ueber Myocarditis, etc., 1880; *also*, Ztschr. f. Heilk., 1880, i. p. 255. **Neumann:** Charité Ann., viii. 1883, p. 246. **Notta:** Union méd., Par., xxxvii. 1884, pp. 549, 561. **Peabody:** Med. Rec. N. Y., xxii. 1882, p. 129. **Pye-Smith:** Trans. Path. Soc., xxviii. 1877, p. 334. **Ribbert** (Experimental): Fortschr. d. Med., iv. 1886, p. 1. **Rosenbach** (Diphtheritic): Arch. f. path. Anat., lxx. 1877, p. 352. **Sanders (W. R.):** Ed. Med. Journ., xiv. 1869, p. 673. **Stevenel:** Contribution à l'étude de la myocardite interstitielle, etc., 1882. **Tenneson:** Union méd., xxxv. 1883, p. 493. **Turner:** Trans. Internat. Med. Cong. Lond., 1881, i. p. 427. **Virchow:** Charité-Ann., iv. 1879, p. 793; *Ibid.*, v. 1880, p. 723. **West:** Lancet, 1886, i. p. 196. **Pfeiffer:** Die acute Entzündung d. Herzmuskels, 1887.

Aneurism of Heart.

511. This is not a very common disease. Wickham Legg (No. 185, 1883, ii. p. 199) records three cases out of one thousand eight hundred and ninety *post-mortem* examinations made by himself.

Heschl (quoted by Legg) places the proportion at one to two hundred, and Willigk (quoted by Legg), at one to one hundred and seventy-seven. It is, however, questionable whether the disease, in all the cases recorded by Heschl and Willigk, was true aneurism.

The **left ventricle** is almost invariably the side affected; and a large proportion of the cases have their seat at the apex. Legg (*loc. cit.*) found from his statistics that in fifty-nine of his cases it was at the apex, thirty-one at other parts of the ventricle.

The aneurism has occasionally been found in the **septum ventriculorum** (see Zahn, No. 13, lxxii. 1878, p. 206). The *pars membranacea* is that which suffers. The sac forms a more or less evident depression, and bulges from the left into the right cavity.

The ventricle may sometimes be so attenuated and dilated, that it becomes almost aneurismal throughout. Ferguson (No. 199, xxiv. 1883, p. 75) relates a case of this kind. The muscular fibre of the left ventricle had entirely disappeared in some localities, its place being taken by fibrous tissue.

The pouch varies in size from that of a filbert up to a large cocoa-nut (Southey, No. 192, xxvi. 1875, p. 43). It usually has a lining membrane composed of the stretched endocardium, and the contents are often old laminated clot with a more recent coagulum. There is, sometimes, a narrow neck leading from the cavity of the ventricle into that of the sac, at other times the orifice is very large.

Bristowe (No. 192, v. 1853, p. 93) describes an example of the disease where the opening was oval in shape and half as wide again as the orifice of the mitral.

Dowse (No. 192, xxvi. 1875, p. 28) relates a case where a cardiac aneurism, located at the base, had opened into the pulmonary artery; and Hayden (No. 288, p. 761), one in which an aneurism of the root of the aorta had formed a communication with the conus arteriosus of the right ventricle.

Terminations.—The sac, sooner or later, ruptures into the pericardium, causing fatal hæmorrhage. In other cases, the person dies from the mechanical interference caused by the sac to the movements of the organ; while the disease may terminate in yet a third issue, namely, the spontaneous calcification and partial obliteration of the sac (Wilks, No. 192, viii. 1856-57, p. 103; Townsend, No. 192, xxiii. 1871-72, p. 96).

Causes.—Local destruction of the muscular fibre from any cause may lead to aneurism, and the left ventricle, which is most often diseased and in which the blood pressure is highest, naturally becomes the usual seat of the protrusion. Local softening of the muscular fibre, caused by disease of a branch of the coronary artery, is a common cause of acute aneurism. So, also, is suppurative myocarditis, when circumscribed. Chronic fibrous myocarditis predisposes to it only when the heart wall is thin, not when it reaches a great thickness.

Literature on Aneurism of Heart.—**Arnott:** Trans. Path. Soc., xix. 1867-68, p. 149. **Barlow:** Trans. Path. Soc., xxvi. 1875, p. 65. **Bell:** Lancet, 1878, i. p. 723. **Bristowe** (Obstruction of Aorta through A.): Lancet, 1881, i. p. 131; *also* (A. of i.

Vent.), Trans. Path. Soc., v. 1853, p. 93. **Canton** (Apex of Vent.): Trans. Path. Soc., xii. 1861, p. 69. **Dowse** (Base of p. Art.): Trans. Path. Soc., xxvi. 1875, p. 28. **Ferguson** (with Fib. Induration): N. Y. Med. Rec., xxiv. 1883, p. 75. **Hughes**: Phila. Med. Times, xiv. 1883-4, p. 439. **Ingals**: Med. Rec., N. Y., xx. 1881, p. 313. **Jacquet**: Progrès méd., xii. 1884, p. 172. **Legg**: Med. Times and Gaz., 1883, ii. p. 199; *also*, Some account of Cardiac Aneurisms, 1884. **Murchison**: Trans. Path. Soc., xxiii. 1871-72, p. 54. **Peabody** (A. with Fibroid Degeneration): Med. Rec., N. Y., xix. 1881, p. 468; *Ibid.*, xxi. 1882, p. 552. **Peluet**: Des anévrysmes du cœur, 1867. **Quain**: Trans. Path. Soc., iii. 1850, p. 80. **Schattuck**: Boston M. and S. Journ., xc. 1874, p. 405. **Schmidt**: N. Orl. M. and S. Journ., xi. 1883-4, p. 331. **Sharkey**: Trans. Path. Soc., xxxvi. 1884, p. 133. **Simon**: Berl. klin. Wochnschr., ix. 1872, p. 537. **Southey**: Trans. Path. Soc., xxvi. 1875, p. 43. **Strange**: Lancet, 1861, ii. p. 445. **Thurnam**: Med. Chir. Trans., xxi. 1838. **Townsend**: Trans. Path. Soc., xxiii. 1871-72, p. 96. **Wilks**: Trans. Path. Soc., viii. 1856-57, p. 169; Brit. Med. J., 1882, i. p. 39. **Zahn**: Arch. f. path. Anat., lxxii. 1878, p. 206.

Syphilitic Disease of the Heart.

512. The fibrous form of myocarditis appears to be sometimes of a syphilitic nature. Cases have been recorded by Dickinson (No. 192, xiii. 1861-62, p. 60), Greenfield (No. 192, xxvi. 1874-75, p. 58), and many others,[1] where the history pointed to a syphilitic origin. (See Bibliography.)

Kantzow (No. 13, xxxv. 1866, p. 211) met with the heart of an infant in which there was a tumour projecting into the right ventricle. On the tumour being examined by Virchow, it proved to be a myoma containing syphilitic miliary gummata. Virchow regarded the tumour as being a muscular hyperplasia due to syphilitic interstitial myocarditis.

Literature on Syphilitic Disease of Heart (see also Myocarditis).—**Ehrlich**: Ztschr. f. klin. Med., 1879, i. p. 378. **Graeffner**: Deut. Arch. f. klin. Med., xx. 1877, p. 611. **Haldane**: Edin. Med. J., viii. 1862, p. 435. **Henderson**: Trans. Path. Soc., xxxiv. 1882-83, p. 53. **Janeway**: Med. Rec., N. Y., vii. 1872, p. 304. **Kantzow**: Arch. f. path. Anat., xxxv. 1866, p. 211. **Legg**: St. Barth. Hosp. Rep., viii. 1872, p. 183. **Leyden**: Deut. med. Wochnschr., ix. 1883, p. 419. **Mannino** (Syphilitic Myocarditis): Gior. ital. d. mal. ven., Milano, xxii. 1881, p. 321. **Pasteur**: Brit. Med. J., 1887, i. p. 14. **Pepper**: Phila. M. Times, vii. 1876, p. 137. **Rollet**: Dict. encycl. d. sc. méd., xviii. 1876, p. 693. **Virchow**: Allg. Wien. med. Ztg., iv. 1859, pp. 62, 67.

Calcification of the Heart.

513. Local deposits of calcic matter are not uncommon where there has been a patch of fibrous thickening, especially if it be adjacent to an endocardium altered by chronic endocarditis. It sometimes happens that the calcification is more extensive. The whole auricle, for instance, may be transformed into a calcic shell—a condition which, so far as one can judge, may for long be compatible with the organ discharging its functions.

The calcified part often becomes fatty previous to its infiltration with the earthy salts.

[1] Cases have even been described (Henderson, No. 192, xxxiv. 1882-83, p. 53) in which a gumma has been found embedded in the sclerous newly formed tissue.

TUMOURS.

514. The heart is one of the organs which is least commonly the seat of the neoplasmata. Those which are found in it are chiefly **tubercle, cancer, myoma, secondary cancer,** and **hydatids.** The myomata are, as a rule, congenital (see Bibliography). Sarcomata, which implicate the heart, generally arise in the mediastina or lung, and grow into it along the large vessels. The heart, however, very often escapes, even when the pericardium is thoroughly infiltrated.

Literature on Tumours of Heart.—**Albers** (Lipoma): Arch. f. path. Anat., x. 1856, p. 215. **Banti** (Lipoma): Sperimentale, Firenze, lviii. 1886, p. 237. **Da Costa** (Tubercle): Proc. Path. Soc. Phila., ii. 1860, p. 34. **Gernet** (Lipoma): Arch. f. path. Anat., xli. 1867, p. 534. **Gilman** (Tubercle): N. Y. Med. Gaz., ii. 1842, p. 385. **Goodhart** (Hydatid): Trans. Path. Soc. Lond., xxvii. 1876, p. 72. **Handford** (Fatty): Lancet, 1887, i. p. 173. **Hirschsprung** (Tubercle): Jahrb. f. kinderheilk., xviii. 1882, p. 283. **Josso** (Myoma?): Gaz. méd. de Nantes, ii. 1883-4, p. 124. **Kantzow** (Syphilitic Myoma): Arch. f. path. Anat., xxxv. 1866, p. 211. **Kelly** (Hydatid): Trans. path. Soc., xx. 1868-69, p. 145. **Kolisko** (Congenital Myoma): Med. Jahrb. Wien., ii. 1887, p. 135. **Martinotti**: Gazz. d. clin. Torino, xxiii. 1886, p. 65. **Maschka**: Prag. med. Wochnschr., v. 1880, p. 495. **Moxon** (Hydatid): Trans. Path. Soc., xxi. 1870, p. 99. **Payne** (Cancerous Endocardium): Trans. Path. Soc., xxii. 1870-71, p. 125. **Peacock** (Hydatid): Trans. Path. Soc. Lond., xxiv. 1873, p. 37. **Pietroni** (Lipoma): Boll. d. sez. d. cult. d. sc. med. n. s. Accad. d. fisiocrit di Siena, v. 1887, p. 101. **Puth**: Ein Fall v. tuberkulösen Herztumor, 1882. **Schöffler**: Ueb. die Tuberculose d. Herzfleisches, 1873. **Virchow** (Cavernous Myoma): Arch. f. path. Anat., xxx. 1864, p. 468; *also*, Sitzungsb. d. phys. med. Gesellsch. zu Würzburg, 1882, 22. **v. Recklinghausen** (Tubercle): Arch. f. path. Anat., xvi. 1859, p. 172. **Wagner** (Tubercle): Arch. d. Heilk, 1861, ii. p. 574. **Waldvogel**: Ein Fibrom des Herzens Göttingen, 1885.

MALFORMATIONS.

(*See Malformations generally.*)

CHAPTER XXXIX

THE HEART—(*Continued*)

Diseases of Endocardium

NORMAL STRUCTURE

515. The endocardium is composed of a thin elastic layer internally, on which lies a single film of polygonal endothelial cells. Outside of this is a second layer, made up of nucleated white fibrous tissue, which is united to the myocardium by means of loose areolar bundles and yellow elastic fibres. In the auricles, the elastic fibres are more developed than elsewhere. The *pars membranacea septi* is said to contain smooth muscular fibres (Krause).

The cusps of the valves may be regarded as reduplications of the endocardium. The atrio-ventricular cusps contain striated **muscular fibre,** which in the adult pierces into them for one-third of their radial distance, and which is connected with the muscle of the auricles. In the fœtus, the valvular muscle is much more fully developed (Langer). The semi-lunar cusps do not appear to possess any muscle; but both they and the atrio-ventricular enclose much elastic tissue.

The greater part of the endocardium is free from **vessels.** Langer (No. 12, lxxxii. Ab. iii., H. i.-v. 1880, p. 208) and Coen (No. 14, xxvii. 1886, 397) agree, that in the perfectly healthy adult heart of Man the semi-lunar cusps are destitute of blood-vessels, and that the atrio-ventricular cusps, on both sides of the heart, possess blood-vessels merely in their upper portions. Langer says, that both in the fœtus and in the adult, they accompany the muscular fibres. The muscular fibres in the adult valve, however, become much retracted, and the vessels consequently ramify through a much less extent of the cusp than during intra-uterine existence and early infancy. The only part of the endocardium proper which contains blood-vessels is the loose areolar tissue uniting it to the muscle; it is otherwise devoid of vessels.

An important point, upon which all workers on the subject of the vessels of the endocardium are at one, is that the edges of the cusps, which are the commonest seats of acute endocarditis, are absolutely free from vascular supply (Luschka, Langer, Martin, Koester).

The endocardium is supplied with abundance of **lymphatics,** which pierce into the valves.

Between the heart muscle and endocardium is a **plexus of nerve fibres,** derived from the coronary plexuses, and free from nerve cells (Krause). Small twigs run from it into the adjacent endocardium.

ENDOCARDITIS (*ἔνδον, within, and κάρδια, the heart.*)

516. **Definition.**—*An inflammation of the endocardium, usually commencing acutely or subacutely, and liable to terminate rapidly in a fatal issue, or to occasion permanent injury to the valves.*

CLASSIFICATION.

Attempts have been made to classify the disease from an anatomical,[1] organismal, or other basis. Such classifications are, however, all more or less artificial and unsatisfactory. The disease in most cases is to be regarded more or less as a complication of some general affection, such as rheumatism, gout, or septic fever, and it therefore seems perhaps more advisable to describe each variety accordingly, reserving the term *idiopathic* for cases which cannot be traced to any such initiatory disease.

RHEUMATIC ENDOCARDITIS.

STATISTICAL.

517. Of all causes of endocarditis, acute rheumatism stands out pre-eminent from its frequency. According to Hayden (No. 288, p. 304), the statistics of English physicians, such as Fuller, Sibson, Budd, Latham, etc., agree pretty closely in indicating, that in about every two out of three cases, endocarditis forms a complication of acute rheumatism.

Rosenstein (No. 206, vi. p. 85) quotes Bamberger as assuming a percentage of 20, Lebert of 17·1, Wunderlich of 15·7, and Roth of 12·6. It may be combined with *pericarditis,* or sometimes even with *myocarditis.* Out of thirty-four cases recorded by Sibson (No. 6, 1870, ii. p. 161) in which there was cardiac complication, four-fifths were of the nature of endocarditis, one-tenth pericarditis, and one-tenth peri- and endocarditis. The large majority of cases occur in individuals under *thirty years of age,* and this also holds good for rheumatic pericarditis. As a rule, there is not much difference as regards *sex,* some

[1] See text-books of Orth, Birch-Hirschfeld, and Sansom, No. 295, etc.

statistics showing a slight preponderance in the female. It has sometimes been held, that the occurrence of endocardial complication in acute rheumatism is related to the amount of *pyrexia* and *implication of the joints*, a view that is regarded by Sansom as untenable (No. 295, p. 23).

SITES.

518. The left side of the heart is that which is almost always exclusively affected in the **adult**, but a competent reason for this has as yet utterly failed. So rare is an endocarditis on the *right* side, that instances of it are often regarded as pathological curiosities.

Fœtal Endocarditis is more common on the right than on the left side, hence many instances of right-sided disease in the adult are supposed to date back to intra-uterine existence.

Bramwell (No. 297, 1886, p. 419) considers, that endocarditis is more common on the right side of the heart than is generally supposed, and explains the absence of signs of it after death, by the inflammation having left no trace of its existence.

Malignant endocarditis, no doubt, is comparatively common on the right side, when the disease is caused by a peripheral source of contamination, but there are grave reasons for doubting whether the statement can be upheld when applied to endocarditis in general. It is also questionable whether an attack of endocarditis ever passes off without leaving some pathological residuum in the shape of an alteration in the thickness, lustre, etc. of the membrane. That the tuberose gelatinous swellings of the valves on the right side, to which Bramwell refers as indicating a former endocarditis, are in any way connected with the disease, may be reasonably called in question. They are to be seen in almost any heart, and in most cases are the remains of fœtal structures (Albinis nodules). It is possible, as Moxon suggests, that friction may cause them to become enlarged.

Parrot (No. 4, i. 1874, p. 538) describes small *hæmatomata* on the edges of the cusps in infants. These, he states, organise and constitute nodules later in life. He can hardly regard them as of pathological significance.

Literature on Diseases of Right Side.—**Baumel**: Des lésions non congénitales du cœur droit et de leurs effets, 1883. **Bischoff**: Die Erkrankungen an d. Mündung d. Pulmonalarterie, 1873. **Bristowe** (Detachment of Vegetation, Impact in the Pulmonary Artery): Trans. Path. Soc., x. 1858-9, p. 114. **Brochier**: Contribution à l'étude de l'insuffisance tricuspide relative, 1878. **Burroughs** (Obliteration of Tricuspid): Boston Med. and Surg. J., xcix. 1878, p. 610. **Church** (Ulceration and Disorganisation of the Pulmonary Valve): Trans. Path. Soc., xix. 1868, p. 147. **Eichorst** (Acute Endocarditis of Pulmonary Artery Valves): Charité-Ann., ii. 1877, p. 240. **Fenwick**: Trans. Path. Soc., xxxii. 1881, p. 42; *Ibid.*, xxxiii. 1881-2, p. 64; *Ibid.*, xxxiv. 1882-3, p. 35; *also*, Lancet, 1881, i. p. 653; *Ibid.*, 1882, i. p. 475. **Marchesi**: Étude sur les altérations de la tricuspide, 1877. **Robinson**: Bull. N. Y. Path. Soc., 1881, i. p. 108.

MORBID ANATOMY AND HISTOLOGY.

519. **Appearances during the Acute Stage.**—It must be borne in mind, as before stated, that the endocardium in the healthy state is a structure almost devoid of vessels, and that its inflammation is to be reckoned in the same category as that of the cornea, of cartilage, and of the inner coat of the arteries. Even in acute endocarditis,

there does not seem to be any new formation of blood-vessels, although, when it becomes chronic, they may become abundant enough in the valves and elsewhere.

Langer (No. 13, cix. 1887, p. 469) says that, in acute endocarditis, he has never been able to recognise, even in the mitral, any vessels which could be regarded as newly formed. The semilunar valves retain their natural non-vascular condition as in health.

What then is the earliest manifestation of the disease? A milky opacity of the membrane appears to be the first sign visible to the naked eye. It is caused by the commencing accumulation of inflammatory products in its lymph spaces, and by the precipitation of granular albumin (cloudy swelling) in the tissue elements. It spreads out diffusely, and ends insensibly in the parts of the endocardium which are not inflamed. It is analogous to the milky opacity of the cornea accompanying acute keratitis. Hæmorrhages into its substance are also sometimes seen.

The cloudiness is followed by a thickening of the membrane, through the increased accumulation of inflammatory materials within it.

Microscopic Examination.—The number of small round cells in the part is vastly augmented. They appear to be in great measure derived from the proliferation of the connective tissue corpuscles. At the focus of greatest inflammation, they are aggregated in a mass, but elsewhere, stretch out in lines or spindle-shaped spaces into the surroundings.

The cell infiltration is chiefly located in the inner dense fibrous layer, but the areolar tissue uniting this to the myocardium also participates; and, indeed, the intermuscular septa for some distance into the substance of the myocardium are similarly all more or less infiltrated. The bundles of white fibrous tissue appear to become homogeneous and to be absorbed in great part as the disease advances.

The cellular effusion accumulates irregularly within the substance of the endocardium, and at the points where the concentration is greatest, the endocardium is forced outwards in little microscopic papilliform projections—a step preliminary to the outgrowth of vegetations.

Over these, at first, the delicate layer of elastic fibres which underlies the endothelium becomes stretched. The endothelium next desquamates, and very soon afterwards, the elastic layer breaks up and is destroyed.

A series of minute abraded projections, composed of small round cells, now covers the affected part, and **fibrin** begins to coagulate upon these. It does not take the form of a network, but is precipitated in dense wavy or tuberose masses having a granular structure. Within the fibrinous deposits, masses of **micrococcus** may occasionally be detected, but it must be remembered that the fibrin itself may

easily be mistaken for them, if means are not adapted to confirm the diagnosis.

The little protuberance is without blood-vessels; were it provided with them it might be called a granulation. It nevertheless continues growing, and projects from the endocardium into the cavity of the heart, being now known as a **vegetation.**

FIG. 193.—SECTION OF SMALL VEGETATION FORMING PART OF A FRINGE ON AN AORTIC CUSP (×50 DIAMS.)

(*a*) Substance of cusp; (*b*) the highly nucleated stem of the vegetation; (*c*) the fibrinous deposit on its extremity (Perosmic acid and Farrants').

Several minor protuberances, of a similar granulation-like texture, next begin to shoot out from its free extremity, so that by the time it has become a naked-eye object, a bunch of secondary vegetations may be found adhering to the single original stalk.

The round cell elements composing the mass, by the time that the vegetation is recognisable as a macroscopic object, have in part become organised. They have thrown out a fibrous matrix, so that now the body presents the appearance of a somewhat coarsely fibrous, warty,

tumour. The stem meanwhile tends to become attenuated and constricted, while the free extremity is increasing its secondary offshoots and taking on a fimbriated character.

By the time that the vegetation has assumed a fibrous appearance, the disease has become more or less subacute, and while in this condition, numbers of blood-vessels can occasionally be seen at its base and running for some distance into its substance.

Koester (No. 13, 1878, p. 275) was able to inject a rich network of blood-vessels in a nodular thickening on an aortic cusp. Langer (No. 13, 1887, p. 470) has found that the vessels in chronic endocarditis constitute, in many instances, a rich plexus, both on the aortic and on the mitral cusps, those of the chordæ tendineæ anastomosing with the latter. As shown by his beautiful injections (*loc. cit.*, Pl. xiii.), the vessels are abundant on the ventral aspect of the aortic cusps, and on the whole of the auricular aspect of the mitral. The tricuspid may similarly become vascularised, but in a minor degree. The edges of the aortic cusps, the corpora Arantii, and, indeed, any part in which much thickening has occurred, contain more blood-vessels than others.

Martin (No. 107, 1886, i. p. 296) also states that vessels may develop in the thickened membrane.

Subsequent Changes.—The thickened endocardium is extremely liable in time to become *atheromatous*. Yellow patches show themselves upon the sclerous tissue, and frequently the base of a vegetation is also the seat of the degeneration. The narrow attachment of the vegetation is thus liable to be weakened, with the result that, occasionally, it is whipped off by the circulating blood and carried away in the systemic circulation. The stump left on the endocardium afterwards contracts and heals, leaving a more or less puckered cicatrix. The thickened endocardium, in the intermediate parts, also cicatrises and contracts, thereby bringing about the deformities of the valves which are so much to be dreaded.

The atheromatous patch may calcify, giving rise to a stone-like nodule or scale. It sometimes happens that the base of the aortic or the cusps of the mitral become converted into a complete calcareous ring.

If a calcic scale become detached, or if the atheromatous patch soften—which it has a decided tendency to do—an **ulcer** is left at the part. Such chronic ulcers are common in cases of protracted endocarditis. They must not be mistaken for the ulcers of *acute septic endocarditis*. They seem to rank parallel with the atheromatous ulcers found, often co-existently, in the aorta or in the other large arteries.

When the ulcer is located on the endocardium between the aortic and mitral, it may destroy one layer of the membrane and then undermine the surrounding parts for some distance. If it be situated upon a valve, and if it be superficial, it is liable to cause valvular aneurism; and if the destruction pierce deeper, actual perforation may follow.

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Endocarditis from Gout.

520. A large proportion of individuals who suffer from endocarditis are constitutionally gouty. The endocarditis, however, does not usually appear during an acute attack. Concretion-like masses of urate of soda are sometimes met with in such hearts, and it would almost seem as if the inflammation of the endocardium were directly induced by its deposition, just as in the case of the joints and fibrous tissues.

Malignant Endocarditis.

521. **Definition.**—*A disease characterised by an acute inflammation either of the left or right side of the heart, or of both; accompanied by fever of a typhoid nature; arising in connection with a source of septic infection; and usually running a rapidly fatal course.*

HISTORICAL.

Our knowledge of the disease dates back to the year when Kirkes' famous paper (No. 34, xxxv. p. 281; No. 19, lxxx. 1853, p. 119), "On some of the principal effects resulting from the detachment of fibrinous deposits from the interior of the heart, and their mixture with the circulating blood," made its appearance. This paper in fact forms the basis of the whole literature of embolism and pyæmia. Its author showed, for the first time, that vegetations may be detached from the valves and be carried into distant organs, and that they may break down and cause a poisoning of the blood from their granular detritus being spread widecast.

A few years later, the disease was inquired into by Virchow (No. 13, ix. 1856, p. 307; No. 129, 1862, p. 458 *et seq.*; No. 236, 1872), Lancereaux (No. 204, 1862), Charcot and Vulpian (No. 204, 1862), and others, and its close relationship to, if not identity with, pyæmia was established.

As the subject of *disease germs* began to develop, the disease in question became singled out as one in which probably micro-organisms played an important part. Quantities of granular matter, in masses, had previously been detected by Rokitansky, Kirkes, and Virchow, lying within the morbid parts; but the nature of this granular matter

remained undefined until Winge (No. 298, ii. No. 36, ii. 1870, p. 95) discovered the leptothrix felt-work of a fungus growing in the thrombi attached to the aortic valve of a man who had died from acute endocarditis excited by an ulcer upon the foot. This could not have been of *post-mortem* growth, as it is stated that the body was frozen quite stiff.

Heiberg (No. 13, lvi. p. 407) next described the case of a puerperal woman who died with symptoms of puerperal pyæmia, and in whom he found ulcerative endocarditis with the same leptothrix chains of organisms in the thrombi upon the mitral, along with infarcts and abscesses of the spleen and kidneys. He believed that these were not of *post-mortem* formation.

In justice, however, it ought to be stated that Virchow (No. 129, 1862, p. 708) had previously observed two cases in which micro-organisms were present on the inflamed endocardium. In the one, they took the form of zooglœa masses, in the other, that of vibrios and fungus-like structures. It is probable, however, that the latter had developed after death, as the body had commenced to putrefy.

Subcutaneous inoculations made from Winge's case on rabbits were without effect; and those made from Heiberg's case resulted only in the formation of a caseous abscess. Koester (No. 13, lxxii. 1878, p. 268) and Klebs (No. 104, ix. 1878, p. 59) showed, that the granular matter on the surface of the affected parts was composed of *micrococcus*, the latter concluding that the organismal invasion constituted the initial stage in the disease.

Since then the disease has been the subject of wide inquiry by a host of observers. (See Bibliography.)

NOMENCLATURE.

522. The designation here adopted ,namely, that of **Malignant Endocarditis,** was given to it by Virchow. It has been adopted by Osler and others, and seems to be preferable to that of **Ulcerative Endocarditis,** for the reason, that the endocardium need not necessarily be ulcerated. It was also called **Diphtheritic Endocarditis** by Virchow, in the wide acceptation of the term, that is to say, in the sense of its belonging to the diphtheritic class of diseases. It must be remembered, however, that it is not a common accompaniment of ordinary diphtheria of the fauces. The name **Arterial Pyæmia** was given to it by Wilks, and, in France, it is often known as **L'Endocardite vegetante ulcereuse.**

GENERAL PHENOMENA OF THE DISEASE.

523. There is often an **open putrefying wound** in some peripheral part, or the subject of the malady may be a woman with

parametritis following delivery; while, in yet other cases, apparently, no such source of contamination is to be discovered.

The disease may also be complicated with **pneumonia** (Osler), **meningitis** (Greenfield), **enteritis** (Bristowe), etc., hence it is practically impossible to tabulate any line of symptoms as indicative of it, seeing that they depend in great part upon the organs affected, and that these are seldom alike in every case.

The patient, as a rule, however, begins to suffer from shiverings, sweating, high temperature, delirium, etc.; or the symptoms may have manifested themselves suddenly, in a person the subject of old cardiac disease. Death takes place, in most cases, before long, the period ranging from a few days up to six months.

MORBID ANATOMY AND HISTOLOGY.

The body tends to premature putrefaction. The pericardial sac usually contains more liquid than in health, or there may be coexistent pericarditis. Both sides of the heart may be affected, but it is more often met with on one side only, and that usually the left. It is, however, the form of endocarditis which most commonly attacks the right side, because the exciting agent is frequently traceable to the organisms of putrefaction absorbed from a distant wound. As Lancereaux (No. 107, 1873, i. p. 673) remarks, the lesions are always more circumscribed in malignant endocarditis than in endocarditis due to rheumatism.

Within the right chambers, and extending into the pulmonary artery, there is often a greenish coloured clot, and similar clots are sometimes met with on the left side. Attached to the edge of one or more of the valves are vegetations, evidently of recent origin. They differ from those met with in ordinary rheumatic endocarditis, in being more fleshy—like pieces of a sarcoma tumour. Their surface usually has a gray colour, or greenish coloured clots may be attached to it.

At other parts, in certain cases, the endocardium is distinctly abraded, or a deep **ulcer** may be situated upon it. In many examples, however, there is no ulceration. The ulceration is most evident where the acute disease has fastened upon an old sclerous part of the membrane. Under such circumstances, a valve may be perforated or torn to shreds, so that little is left of it.

If the endocarditis be right-sided, **pyæmic abscesses** may be expected in the lungs; but, if left-sided, the lungs are usually simply œdematous, the liquid having a greenish colour when squeezed out, and being mixed with catarrhal mucus from the bronchi.

Infarctions are common in the spleen, kidneys, and liver; they sometimes liquefy so as to constitute pyæmic abscesses. **Meningitis** has occasionally been noticed.

Septic thrombi may be found filling some of the large veins or arteries. **Vegetations** are not common in the arteries, but if a large

artery, like the aorta, be abraded from the presence of atheromatous degeneration, vegetations in all respects alike with those in the heart may sprout out from the lacerated parts.

Microscopically examined, the vegetations in the heart and other parts (see Fig. 194) will be found to be distinct outgrowths of the tissue to which they are attached. Their surface is covered with fibrin, within

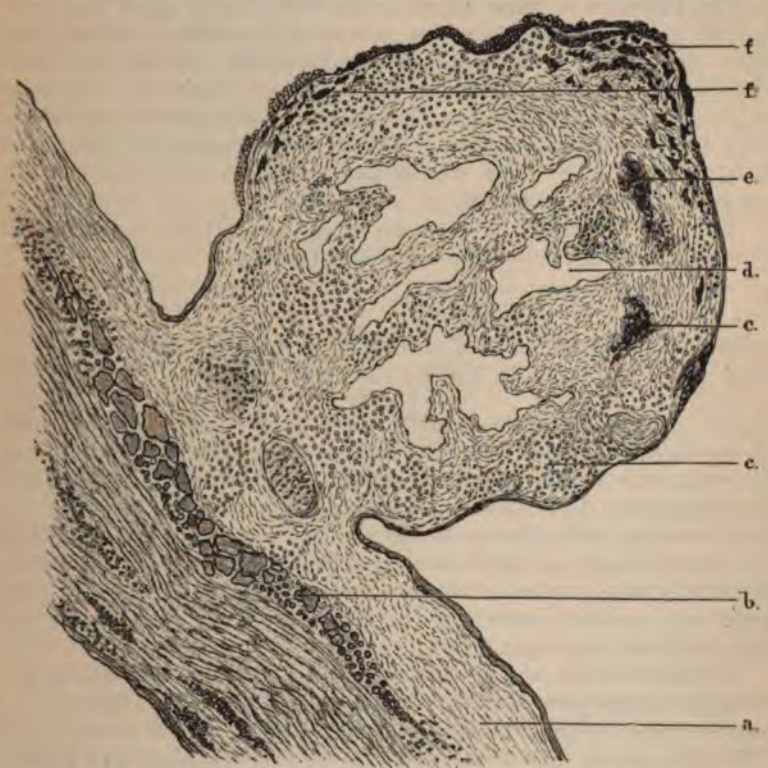

FIG. 194.—SEPTIC VEGETATION GROWING FROM AN ATHEROMATOUS AORTA (×50 DIAMS.)
(*a*) Coats of aorta; (*b*) atheromatous deposit in same; (*c*) nucleated deposit in vegetation mass; (*d*) a space in centre of vegetation; (*e*, *e*) substance of the vegetation with hæmorrhages in it; (*f*, *f*) deposits of micrococcus on its surface (Gentian violet and gum dammar).

which lie masses of **micrococcus,** or the entire surface of the vegetation may be coated with a continuous layer of the same. Within the vegetation mass, small cavities are sometimes seen, whose walls frequently have dépôts of micrococcus adhering to them; and isolated zooglœa heaps of micrococcus may, here and there, be encountered scattered throughout its texture.

Valves Affected.—Osler (quoted by Sansom) states, that his records show the mitral valve to have been alone affected in 77 cases;

aortic valves alone in 53; aortic and mitral together in 41; heart-wall in 33; tricuspid valve in 19; pulmonary valves in 15.

Identification of the Disease.—Every case of ulceration of the endocardium is not of a malignant type. Of late there has been too great a tendency to refer other forms of ulceration to the malignant affection.

The presence of micro-organisms in the affected parts has been looked upon as a diagnostic sign, and it is astonishing to find how often these have been described as abundantly present where no evident source of contamination prevailed—so much so, that there is just the suspicion that granular masses of fibrin may occasionally have been mistaken for them. On careless examination, this could easily happen; the fibrin masses are sometimes very like zooglœa accumulations of micrococcus.

The whole features of the case ought to be taken into account before pronouncing it to be of a malignant type.

THE ORGANISMS ASSOCIATED WITH ULCERATION OF THE ENDOCARDIUM.

524. It is questionable whether there is any one organism which is invariably associated with the disease. Cornil, Osler, and Wyssokowitsch believe that there are several, each inducing its own train of symptoms. Klebs, Koester, Orth, and others, made out that the organism most often found on the diseased valves was a micrococcus, but since then, it has been discovered that a bacillus may sometimes apparently take its place. By improved methods of fractional cultivation, more accurate knowledge has been obtained of late regarding these different organisms.

In **septicæmic** and **pyæmic** conditions of the body the micro-organisms found have been the following:—Rosenbach's *staphylococcus pyogenes flavus*, *staphylococcus pyogenes albus*, and *streptococcus pyogenes* (No. 299), along with Passet's *staphylococcus cereus albus*, and *bacillus pyogenes fœtidus* (No. 11, iii. 1885, p. 33).

Fraenkel and Saenger (No. 13, cviii. 1887, p. 305) verified the presence of the following organisms in thirteen instances of malignant endocarditis. Some of them are pathogenic and others harmless:—

(1)	Staphylococcus pyogenes flavus (Rosenbach)	7 times.
(2)	Staphylococcus pyogenes albus "	3 "
(3)	Staphylococcus cereus albus (Passet)	2 "
(4)	A non-pyogenic Staphylococcus flavus	1 "
(5)	Bacillus pyogenes fœtidus (Passet)	1 "
(6)	A non-motile, non-pyogenic fœtid bacillus	2 "
(7)	A yellow non-liquefying coccus	1 "
(8)	A non-liquefying white coccus	2 "

In the variety of endocarditis associated with **pneumonia,** Netter (No. 4, xviii. 1886, p. 112) found the *pneumococcus* on the vegetations.

Cornil (No. 300, 1884, No. li.) refers to the *tubercular bacillus* having been discovered in the endocarditis accompanying **pulmonary phthisis**; and a *bacillus* has lately been isolated by Delafield and Prudden (No. 370, p. 266) from a very acute case. In endocarditis complicating purulent inflammation of the bile ducts, caused by gall stones, Netter and Martha (No. 4, xviii. 1886, p. 7) have also found a *bacillus.* On agar-agar, Weichselbaum (No. 188, 1885, No. xli.) cultivated *streptococcus pyogenes*, from the urine, and *staphylococcus aureus* and *albus* and *streptococcus pyogenes*, from the morbid parts, of three persons dying from ulcerative endocarditis.

(For detailed description of these organisms see vol. ii. "Vegetable Parasites.")

The Organisms which are Pathogenic.—Many of the foregoing are undoubtedly harmless, and are mere accidental accompaniments of the disease.

Experiments have of late been made with the view of determining which of them are of pathological significance. From most of these experiments (Rosenbach, No. 104, ix. 1878, p. 1; Wyssokowitsch, No. 13, ciii. 1886, p. 328), it seems to be established that mere wounding of the valve will not induce ulcerative endocarditis, provided the instruments employed in the operation be sterilised.

Both **staphylococcus pyogenes aureus and streptococcus pyogenes** have been found by Wyssokowitsch (*loc. cit.*) to induce endocarditis, when injected into a vein of the ear in the rabbit, *after the valves of the heart had been wounded* by the introduction of a sound through the right carotid artery. When injected into the lung, they did not call forth endocarditis, and were well borne by the animal.

He believes that streptococcus p. is the morbific agent in puerperal endocarditis, and that although staphylococcus p. aureus is very frequently present, and is in all probability one of the organisms most active in exciting malignant endocarditis, yet, that it is by no means the invariable cause.

He (*loc. cit.*) finds that a coccus separated by Nicolaier from soil, by inoculation of mice, induces endocarditis in rabbits under the same circumstances.

He has thus discovered that there are three organisms, the introduction of any of which into the circulation is followed by positive result, when a valve has previously been wounded. He affirms, on the contrary, that *micrococcus tetragenus* and *bacillus pneumoniæ* (Friedländer's diplococcus) are inert. It should, however, be stated that Netter (No. 4, xviii. 1886, p. 106) found the pneumococcus present in the heart in pneumonic endocarditis, and has been successful in inducing the disease in animals, with pneumonic products.

Perret and Rodet (No. 150, p. 778, 1885) have successfully inoculated dogs with distilled water in which pieces of endocardium affected with ulcerative endocarditis had been beaten up.

MANNER IN WHICH THE ORGANISMS GAIN ENTRANCE TO THE VALVES.

525. Klebs (No. 104, ix. 1878, p. 52) held that the organisms invaded the system through **the lung**; that they were carried to the left heart; that in the closing and opening of the valves, they were retained for some time at the meeting points; and that consequently, they took hold of these and fructified upon them. Kœster (No. 13, lxxii. 1878, p. 269) was of opinion that they were carried embolically into the **vessels of the valves**; and, as the valves contain more vessels than other parts of the endocardium, that the choice of these as the favourite seat of the lesions in endocarditis was thus to be accounted for. This opinion would be rather contra-indicated by the facts previously mentioned (p. 594), namely that, in the healthy state, vessels are absent in the semilunar and are very scanty in the mitral valve, and that new vessels have never been found in acute endocarditis. It might, however, explain how old sclerous valves, seeing that they are very vascular, frequently become the seat of an acute attack of endocarditis.

The more general view is that taken by Cornil and Babes (No. 302, p. 302), namely, that they pierce into the substance of the membrane from the surface. This idea would seem to be negatived by the fact that the injection of micro-organisms has usually failed to induce endocarditis, unless where the valve had previously been wounded. Dreschfeld (No. 6, 1887, ii. p. 887), however, has succeeded in cultivating an organism from the vegetations of non-ulcerative endocarditis, which, when mixed with beef-tea and injected into the jugular vein of a rabbit, caused a most extensive and marked outgrowth of vegetations on the mitral and aortic valves. The same streptococcus was found in the vegetations as in the heart from which the virus was taken. It was transferred from one rabbit to another with a like result.

Ribbert (No. 11, iv. 1886, p. 1), in the previous year, had demonstrated that if staphylococcus aureus, after cultivation on potato, be injected into a vein of the rabbit's ear, it has the power of inducing an endo- and myocarditis without the tissues having been wounded.

Methods of Preparation.—Open the heart as carefully as possible, and without any undue squeezing. Cut out the affected parts of the endocardium with a scissors, without allowing water to touch them. Harden in "A," and cut in the freezing microtome, after soaking in "B" freezing fluid. Stain by Gram's method, clarify, and mount in solution of gum dammar or Canada balsam.

Pneumonic Endocarditis.

526. Bouillaud and Legroux, a good many years since, drew attention to the frequent co-existence of acute pneumonia and endocarditis; and attention, in late years, has been more particularly drawn to the connection by Osler (No. 264, i. p. 342; No. 6, 1885, i. p. 578), and Netter (No. 4, xviii. p. 106). Individual instances of the disease have been recorded from time to time by Gulliver, Barth, and others.

The endocarditis comes on during the attack of pneumonia, or in convalescence. Netter believes that the most of these cases are accompanied by a pneumococcus, but states that not every endocarditis which supervenes in the course of a pneumonia is due to this agent. Those who have had an old cardiac lesion previously, are peculiarly predisposed to it. It is a fatal form of endocarditis, death supervening from the fifth to the eighty-sixth day.

It occupies the left chambers of the heart oftener than do the other forms of ulcerative endocarditis, and, more generally, the aortic than the mitral orifice. It is frequently complicated by meningitis, but seldom by embolism, and the lung rarely suppurates.

Netter (*loc. cit.*, p. 112) found the same pneumococcus present on the vegetations seven times, and also throughout the whole substance of the lungs. It is likewise found in the blood.

Other Sources of Septic Endocarditis.

Endocarditis has been found associated with several other diseases, many of which are currently regarded as caused by a micro-organism. Among these may be mentioned **scarlet fever, measles, typhoid,** and **acute osteo-myelitis.** Lancereaux (No. 107, 1873, i. p. 672) has put on record a number of cases in which, apparently, malignant ulcerative endocarditis was due to **paludinic** causes.

As pointed out by Lecorché (No. 107, 1882, i. p. 385), endocarditis is somewhat common in **diabetics.** Whether it be of an organismal nature or not, remains to be seen. Ordinary diphtheria of the fauces is rarely associated with endocarditis.

Finally, it may be asked whether the **rheumatic form** of the disease is organismal, and to this it is difficult to give a direct reply.

Klebs and Koester regarded *all* forms of endocarditis as organismal, and the notion is still adhered to by some observers. Klebs (No. 104, ix. 1878, p. 65) maintained that the cocci in the rheumatic form of the disease were larger than those of septic endocarditis, and that they were imbedded in a gelatinous mass which constituted a capsule for each individual of the group.

Osler (No. 264, 1881, i. p. 345) supports the view that they are present in rheumatic and other forms of endocarditis besides the purely ulcerative form. Micrococci, he says, "abound in all forms of endocardial vegetation—in the warty

outgrowths of rheumatic endocarditis, in the vegetations of old sclerotic valves as well as in the excrescences which develop in the acute ulcerative form."

Fraenkel and Saenger (No. 13, cviii. 1887, p. 310) maintain, that both the *endocarditis verrucosa* and *ulcerativa* are mycotic diseases. The mere failure to find organisms in a particular case, they say, cannot be held as definitely settling that it is not of an organismal type. There is only one form of endocarditis which, they maintain, is not of a mycotic nature, namely, the atheromatous. They would include the sclerous form, were it not as yet a doubtful point as to whether it is not simply the final stage of an E. verrucosa of parasitical origin.

THE ALLEGED ENGRAFTING OF ACUTE ULCERATIVE ENDOCARDITIS UPON AN OLD INDURATED BASIS.

527. It has been said that acute ulcerative disease of a septic nature may seize upon a chronically sclerosed endocardium, and induce a truly septic ulcer upon the old indurated basis.

Paget (No. 34, xxvii., quoted by Osler) is admitted to have first directed attention to the frequency with which chronically sclerosed valves are attacked with acute disease.

Osler (No. 6, 1885, i. p. 467) states that more than three-fourths of the cases of acute malignant endocarditis met with in the Montreal General Hospital, were accompanied by sclerotic changes.

Goodhart (No. 192, xxxiii. 1882, p. 52) found that out of sixty-nine cases of acute ulceration, sixty-one were in hearts affected with chronic fibrous lesions.

It cannot be denied, that there is a certain amount of evidence to support the idea that at least subacute attacks of endocarditis are liable to ensue, from time to time, in a chronically impaired endocardium. Crops of vegetations manifestly of recent origin, are frequently seen sprouting from a rigid and sclerosed part of the membrane, or from a deformed valve. Nor can it be admitted for an instant, that these date back to the same primary attacks of endocarditis which occasioned the chronic thickening, and the only conclusion to be drawn from them is, that they are the outcome of a second attack, coming on after the active inflammatory changes in the membrane have become quiescent.

That the vegetations, abrasions, or ulcers which result therefrom are of a *septic* nature, may be open to doubt. Were the individual under conditions which might tend to induce a septic state of the blood, it is conceivable that the weakened, and it may be wounded, endocardium would constitute a favourable point for parasites fixing upon.

The author recently met with a case of this kind. It occurred in the person of an old woman with a chronically atheromatous, calcareous, and ulcerated aorta. About a fortnight before her death she accidentally received an extensive burn of the back, neck, and shoulders, which resulted in the skin of these parts sloughing. The wound putrefied in spite of antiseptic dressings, and she evidently died from septic poisoning. The aorta was very atheromatous, and wherever an abrasion of

the surface occurred, there was a recent, soft, flesh-like vegetation mass covering it, containing numerous masses of micro-organisms. The heart, which was free from ulceration or endocarditic thickening, did not show any of these vegetations, nor did other vessels whose surfaces were intact. It was only where the deep textures of the vessel were exposed, that they were to be found.

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Idiopathic Endocarditis.

528. As before mentioned (Sect. 516), it is proposed to reserve this term for those instances of endocarditis whose ultimate cause has not as yet been detected. Their number is growing daily less, and, in course of time, the class will probably become extinct.

CHAPTER XL

THE HEART—DISEASES OF ENDOCARDIUM—(*Continued*)

Effects of Endocarditis on the Valves

(1) *AORTIC*

529. It will be remembered, that there is a fibrous ring in the human heart, at the base of the aortic valve, which serves to unite the aorta with the muscular wall of the ventricle. A similar, although more slender, ring is placed at the base of the pulmonary artery.

Pettigrew (No. 78, p. 189) describes these rings thus:—"Each ring consists, as was shown by Reid, of three convex portions. Each convex portion is directed from above downwards, and from without inwards, and as it unites above with that next to it, the two when taken together form a conical-shaped prominence, which is adapted to one of the three triangular-shaped interspaces occurring between the segments of the semi-lunar valves." In some animals, these rings are cartilaginous, and it has even been asserted (Donders) that stellate corpuscles similar to those of cartilaginous tumours occur in Man. Pettigrew (p. 267) says, that they give attachment to the muscular fibres of the auricle, but to almost none of those of the ventricle.

It should be borne in mind that the aortic cusps are often naturally fenestrated at the margin.

During the acute stage, the cusps like other parts of the endocardium become milky, thickened, and opaque, and when the chronic stage sets in, the quantity of fibrous tissue becomes excessive. The parts showing the greatest thickening are at the edge of the cusp, around the corpus Arantii, and in the above-mentioned fibrous ring.

The thickening of the free margins of the cusps causes retraction, followed, in course of time, by its almost inevitable consequence—incompetency. The induration of the fibrous ring at their base, on the other hand, induces narrowing or stenosis of the orifice with its attendant circumstances. The retraction of the aortic cusps is sometimes so extreme that they may come to be represented merely by tense, vocal-cord-like, ridges.

The ulceration which follows the sclerosis of the valves is accompanied by the most disastrous results. It may destroy half their thickness, and thus predispose to valvular aneurism, or it may perforate the entire thickness. In other instances, the cusp presents a ragged appearance—it becomes torn into fragments, and these are sometimes found dangling by an attenuated extremity.

The aortic ring sometimes suffers complete calcification.

One aortic cusp may be unnaturally large and stretched, while the other two may be thickened and retracted. By this means, what would otherwise have been a regurgitant valve may still retain its competency, the one large cusp filling the space left vacant by the other two. This has been explained on the ground of congenital deformity, but the explanation will not always hold good. A more probable theory seems to be that which presupposes it to have been less injured by the endocarditic thickening, and hence to have had increased work thrown upon it.

Vegetations frequently sprout from the aortic cusps, and are most generally located on the margin of the valve, or on its ventricular aspect where the cusps meet. In the latter situation they often construct a fringe-like crescent. They are rarely seen on the aortic surface of the valve, an exemption which is supposed to be derived from there being less friction on the aortic side than on the ventricular.

Indeed, some authors have gone so far as to allege, that endocardial thickening is always due to friction.

Hodgkin (No. 178, iii. p. 439) drew attention to the thickening the endocardium suffers by the rubbing against it of an adjacent chronically indurated portion.

Virchow (No. 129, p. 506) explained the occurrence of endocarditis so frequently upon the valves, by the stretching and friction to which they were subject.

Moxon (No. 59, 1873, ii. p. 622) has been led to believe that the "friction with fibrin clots, together with mechanical strain, make the principal, if not the sole, direct cause of endocarditis; rheumatism and other general states creating only a vulnerability of the fibrous structures so that they cannot resist the irritation of the friction."

Aortic valve disease from acute rheumatism is commoner in men than in women. This is said to be an effect of overstrain upon the cusps.

(2) *MITRAL.*

530. The mitral valve cannot, strictly speaking, be held to consist of two cusps. If it be carefully examined, it will be found that the free edge is perfectly continuous and unattached all round, whereas the aortic cusps are separated by distinct intervals.

The wing-like appendages at each side of the mitral, in animals, are not discoverable in Man.

What is called the posterior cusp of the mitral is much the less movable of the two. This is occasioned by its being shorter than the anterior, and also by the fact that it is bound to the wall of the ventricle

by a complete network of short tendinous cords, which thus effectually prevent its being driven upwards into the auricle during the ventricular systole. The anterior cusp, on the other hand, practically comprises the whole of the endocardium from the base of the aortic downwards. It is, in fact, attached to the part of the aortic ring corresponding to the two anterior aortic cusps. The mobile part of the anterior cusp will, accordingly, be found to be something like three times as extensive as that of the posterior, and, moreover, not being restrained by any tendinous structures other than the chordæ tendineæ of the musculi papillares, it is thus enabled to move through a much larger space than the posterior.

If air be blown from a bellows by gentle puffs into the ventricle, through an incision in the apex, and if, at the same time, the aorta be ligatured, the preponderating freedom of action of the anterior cusp can be beautifully seen. The posterior hardly moves while the anterior is alternately retracted and driven upwards.

The **Musculi papillares** of the mitral arise in two sets, both from the posterior wall of the ventricle, and are placed, one at the right, the other at the left side of the flattened valve. Each set can be roughly subdivided into two main masses, and to these the chordæ are attached.

The **primary chordæ tendineæ** arising from each lateral mass of musculi are from five to seven in number. They soon split up, however, so that at their points of insertion into the cusps they may have increased threefold, and they become correspondingly finer. They are inserted into the right and left sides of the free margin of the flattened funnel-like valve; but both anteriorly and posteriorly the insertions of the fan-shaped expansion, which the mass of chordæ resembles, nearly meet.

The effect of an old endocarditis on the mitral is to cause thickening of all its parts. Not only does the substance proper of the valve suffer, but the chordæ tendineæ, where the disease has been at all extensive, almost certainly participate. The result of this thickening is, that the intervals between the subdivisions of the chordæ become reduced in size and ultimately filled up, so that they come to resemble a solid fibrous pillar rather than an aggregation of isolated bands. At the same time, they are dragged upwards towards the margin of the valve, and so shortened that the tip of the musculi papillares may actually be in contact with the cusps. The posterior wall of the ventricle is also pulled upon, and being thus bound to the sclerosed mitral, will be retarded in its free action.

The mitral has just been described as having a continuous free margin. It, in fact, resembles a collapsed funnel pushed into the ventricle. When the valve has become the subject of chronic thickening, this continuity of the edge causes a peculiar and characteristic deformity. The valve contracts universally so as to narrow the outlet of the funnel. In the majority of cases, the orifice of the valve becomes

transformed into a buttonhole-like slit; in a few, it retains its funnel-like character.

At first sight, it appears as if the adjacent surfaces of the valve had become adherent, but, on more careful examination, it will be seen that this is fallacious, and that the narrowing is, in reality, a result of the universal leather-like thickening of the free margin of the orifice. It is, indeed, questionable whether, under any circumstances, the surfaces either of the mitral or aortic valves become adherent. The condition is often described, but, in most cases, if more carefully examined, the deformity can be otherwise explained. Those cases in which the cusps of the aortic have been described as fused together so as to resemble an inverted funnel, have probably been so congenitally. The constant motion of the valve would, it might be supposed, tend to prevent any such adhesion occurring.

As the mitral is practically continuous, through its anterior cusp, with the aortic, it follows, that any contraction in this cusp will pull upon the latter. It is a question, whether the aortic or mitral might not in this way be rendered secondarily incompetent.

When the mitral is looked at from the auricular aspect, much the best view is had of the amount of deformity which it has suffered. The buttonhole-like shape of the aperture then becomes apparent; and, frequently, tuberous, fibrous, or calcareous masses can be seen projecting from the side of the cusps.

The Vegetations, in mitral disease, are most commonly on the free margin, or on the auricular aspect. When on the latter, they may resemble a narrow fringe, or may be spread out in the wall of the auricle; and often cover a wide area. When outspread in this way, they commonly lie on the left wall of the auricle, that is to say, *opposite the points of entrance of the pulmonary veins.*

The chronically sclerosed mitral is prone to **calcification.** The calcic matter may be deposited in masses or be universally distributed. A large atheromatous and calcareous *plaque*, which materially interferes with the free play of the anterior mitral cusp, is frequently placed in the expansion of endocardium between the two valves. It sometimes happens, that the auricle may be so universally calcified as to resemble a shell-like structure.

(3) *TRICUSPID.*

531. In three typical instances of tricuspid stenosis which lately came under the author's notice, the following was the condition of the valve. The cusps were all thickened, especially at their edges, so that they appeared to be adherent, a fallacy already referred to under mitral disease. The edge of the funnel-shaped aperture had become indurated and retracted, so that its subdivision into three parts had practically been obliterated. The diameters of the orifices were ·9 inch in one example and 1 inch in the other two (normal 1·5 to 1·8 inch). In

all cases, it was accompanied by old standing endocarditic disease of the left side; and, in each of the three, there was evidence to show that the tricuspid disease was not congenital, but had been due to a like cause. In one case, the stumps of vegetations were adherent to the thickened edge of the valve. The valve appeared to be incompetent in them all. In one instance, the mitral alone, in the other two, the mitral and aortic, were sclerosed. The lesions of the left side were far more severe than those of the right. In none of the cases, was there any abnormality of the pulmonary artery orifice.

Rosenstein states (No. 206, vi. p. 150), that stenosis of the tricuspid dates from fœtal life, and Peacock (No. 192, v. p. 67) inclines to a similar view. This was not borne out by the history of two at least of the individuals from whom the above hearts were taken (the history of the third case was unfortunately wanting). There was a distinct record of rheumatic fever a few years before death, and the appearances pointed to an endocarditis supervening in adult life. They were all over twenty-seven years of age.

The disease is more common in females than in males. In the above three cases, two were females and one a male. (See also Greenfield, No. 192, xxvii. 1875-6, p. 113).

(4) *PULMONARY ARTERY.*

532. Inflammatory disease of this orifice is undoubtedly rarer than that of any other. The most remarkable case which the author remembers to have examined, was one in which a huge mass of fimbriated vegetations grew from the cusps, so large as in great part to obliterate the opening. The other orifices were healthy.

EFFECTS OF ENDOCARDITIS ON OTHER PARTS OF THE MEMBRANE.

Patches of thickened endocardium are frequently noticed elsewhere than in the vicinity of the valves. These are liable to become atheromatous or to calcify, or they may ulcerate. Vegetations are occasionally seen sprouting from them, more especially when they are located over a musculus papillaris.

EFFECT OF ENDOCARDITIS ON THE ACTION OF THE VALVES.

533. **Mitral.**—It will be found that, in nearly every example of mitral stenosis, where the rigidity is at all advanced, the valve is also incompetent.[1] Constriction with incompetence, moreover, constitutes, out of all proportion, the commonest form of mitral deformity.

Instances of pure mitral regurgitance are rare, and are usually the effect of dilatation of the ventricle (Balfour). Hilton-Fagge (No. 209,

[1] See also Rosenstein on this subject, No. 206, vi. pp. 125, 161.

iv. p. 609) says that another cause of it, is stretching of the chordæ, whereby the edge of a cusp becomes inverted into the auricle during systole, but emphasises, that the condition is rare. A more likely cause of mitral incompetency without constriction would, *a fortiori*, be where one of the chordæ becomes shortened and drags upon the valve.

From the author's own statistics, it appears that not a single case of mitral defect was referrible to a purely dilated state of the valve. This is to be accounted for by the lax condition of the free margin of the valve allowing of considerable stretching and adaptation to a deficiency. When air is driven into the valve from below, it becomes evident that there is a superabundance of lax tissue at the edge, which, in the natural state, is thrown into folds in a spiral manner (Pettigrew), and which can be expanded when the orifice is dilated, without allowing of regurgitance.

Aortic.—The effect of endocarditis on this orifice depends mostly upon what structure of the orifice is chiefly implicated. *Aortic stenosis* is, in by far the greater number of cases, the result of induration and constriction of the *aortic ring*, whereas *aortic incompetence* follows upon contraction and deformity of the *cusps;* sometimes, it is said, although this is doubtful, upon pure dilatation of the aperture. Constriction of the aortic and of the mitral orifices is thus caused by two different factors. In the former, it is the base of the valve which is involved (the aortic ring), while the cusps may be free; in the latter, it is the edge of the valve, and, usually, a great portion of the substance of the valve itself which occasion the constriction.

As a matter of experience, however, in the *post-mortem* room, it will be found, that *the aortic orifice is rarely constricted without the valve being at the same time incompetent.* The converse does not hold good, for the valve may be decidedly incompetent and the size of the orifice be either normal or greater than in health.

The explanation of the fact that stenosed aortic is almost always accompanied by regurgitance may be twofold, namely, either that the cusps are coexistently implicated with the aortic ring in the sclerosis, or that the constriction of the aortic ring throws them into folds and prevents their accurate closure. In the latter case, the incompetence is often slight.

Tricuspid.—This valve, like the mitral, is in reality a free funnel inserted into the ventricle. The cusp which lies adjacent to the ventricular septum is, like the posterior cusp of the mitral, firmly bound down to the wall of the septum by a plexus of short chordæ. When air is blown into the ventricle, this cusp moves very little, the closure of the orifice being effected mainly by the other two cusps. Of these, the one which lies immediately below the pulmonary artery presents the larger surface, and is the more mobile.

The tricuspid differs from the mitral in being disunited from the base of the semi-lunar cusps. It is, in fact, a purely *atrio-ventricular* structure, while the mitral is an *atrio-ventriculo-aortic* structure.

The tricuspid may be stretched to a great size, evidently without seriously impairing its utility. Simple dilatation of the tricuspid may be present without necessarily any disease of the left side. There is no murmur in most of these cases to indicate that the valve is dilated, nor is there necessarily any of the venous turgescence during life that might *a priori* be expected. If air be blown into the right ventricle, the tricuspid, owing to a slight escape of air from between the cusps, will seldom be found to close with the sharp click that can be elicited from all the other three orifices. This amount of incompetency has been supposed to be the normal condition of all hearts, and *post-mortem* examination would almost point to a still greater incompetency of the tricuspid, through dilatation, being present in many individuals without causing any appreciable physical sign.

There is, admittedly, considerable difficulty in accurately diagnosing tricuspid disease, even where there is a murmur (see Sansom, No. 295, p. 155), but the existence of tricuspid regurgitation without any murmur would be still more difficult of detection. Jugular pulsation is one of the commonest signs of tricuspid regurgitation with a murmur, still, it may be present without any murmur being capable of detection (compare Rosenstein, No. 206, vi. p. 151; and Balfour, No. 289, p. 179).

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The Relative Danger of Valvular Lesions.

534. It has long been recognised that an individual may have a loud left-sided valvular murmur from organic lesion, and not experience any inconvenience from it. Some of these persons live to old age.

Clark (No. 6, 1887, i. p. 372) has tabulated a series of six hundred and eighty-three instances of patients who consulted him for other diseases, and in whom he discovered an unsuspected valvular murmur. Some of the murmurs were mitral, others aortic, and, in a large proportion, the lesion affected both orifices.

It is pretty generally acknowledged that the most dangerous form of valvular disease is aortic regurgitance; at any rate, the patient is more likely to die suddenly from this than from other valvular defects.

In such cases of sudden death, the aortic orifice is often dilated as well as incompetent. On referring to Section 540, and to those immediately succeeding, it will be found, that of all aortic lesions, this is the one which induces greatest dilatation of the other orifices, and that it is followed by the greatest hypertrophy of the ventricular walls, circumstances evidently pointing to strain during diastole from arterial recoil.[1]

There is, however, much difficulty in estimating the relative danger of valvular lesion, owing to no two cases being exactly alike, as regards the nature and extent of the disease, the amount of compensation which has taken place, and the general efficiency of other organs. Reasoning from a theoretical basis, it might be said, that a constricted mitral with an incompetent aortic, ought not to be so dangerous as one in which the mitral is of natural size or dilated. The destructive influence of aortic regurgitance is felt during diastole, when the mitral is open, and hence a narrow mitral ought to allow less regurgitance upon the lung than one which is large.

The result of any valvular injury of the heart, however, must greatly depend on the *strain* put upon the organ, and hence it is probable that the cases referred to by Clark, as without evil issue, would be relatively more abundant among patients in the higher ranks of society than among the inmates of hospitals.

The ill-effect of strain of the systemic muscles will be felt in any valvular disease, but specially so in *aortic regurgitation*. So long as the circulation is tranquil, the patient may go on without being much inconvenienced. The moment the muscles of the trunk are brought into violent contraction, the arterial pressure rises, and the aortic blood consequently recoils with sudden impact upon the interior of the left ventricle, thus predisposing to dilatation with all its attendant disasters.

[1] The mechanism of this is explained in the above Sections.

Balfour (No. 289, p. 71) draws attention to the much greater danger accompanying sudden rupture of one of the aortic cusps, as compared with insufficiency gradually produced by disease. He quotes B. Foster as placing the limit of life in such cases at four and a half years. In ordinary aortic disease, Balfour reckons it at from three months to twenty-five years (*loc. cit.* p. 86).

Effects of Valvular Disease upon the Arterial Blood Pressure.

535. **Experimental.**—Many theories have been held on this subject, all more or less unreliable from being unsupported by experiment. The following results have been obtained by injuring the valves in animals and measuring the pressure at different parts of the arterial system.

Method.—A special valvulotome has been constructed by Klebs for the purpose of injuring the valves. It is pushed into the right carotid artery in order to reach the valves of the left side, and into the right jugular vein in the case of those on the right. The pressure should be estimated by means of a manometer introduced into the carotid or crural artery, and into both simultaneously. The setting up of an endocarditis, in performing the operation, seems to depend more on contamination through unclean instruments than on the actual injury.

Cohnheim (No. 31, i. pp. 38, 39) showed that, if the aortic is rendered completely incompetent in the dog, the defect has no appreciable influence upon the arterial blood pressure. He explains this by supposing the heart to possess sufficient reserve *energy* to drive as much blood into the aorta as when the valve is uninjured. When the aortic is constricted, the same effect follows, and from a like cause. The heart contracts more energetically, and hence drives through the narrow orifice as much blood as would be propelled through a wider orifice by one contracting feebly.

Rosenbach (No. 104, ix. 1878, p. 1), employing dogs and rabbits, found that extensive destruction of the aortic, mitral, or tricuspid does not lower the arterial pressure, indeed a slight rise usually takes place, probably owing to interference with the heart's action in performing the operation. In rabbits which were allowed to live for different periods after the valves were rendered incompetent, the pressure was still uninfluenced. If the orifice of the aorta was narrowed by the introduction of a sound, still no effect followed.

De Jager (No. 49, 1883, ii. p. 142) has obtained the same results in dogs, the subject of artificially induced insufficiency of the aortic, mitral, or tricuspid; but, in rabbits, a fall in the arterial blood pressure was noticed.

It may legitimately be asked, why the arterial pressure should fall in aortic insufficiency. Is the amount of blood which regurgitates into the ventricle at each diastole, sufficient to influence the blood pressure all over the body? If not, and if the heart can still contract with energy enough to drive the blood onwards, and to empty the cavity, it does not seem quite clear why a fall in blood pressure should take place. If the ventricle were to dilate, then the heart would act at a disadvantage; but if undilated, does it lose in propelling power

by being filled from two sources instead of from one? The arterial pressure might sink slightly during the diastole of the ventricle, from the recoil being greater, but would again rise during ventricular systole, especially if the heart contracted more vigorously than when the valve is sound. The maximum arterial pressure would probably not be much influenced.[1]

Influence of Valvular Disease of the Heart on other Organs.

536. It may be said that, practically, any valvular lesion occasions more or less disturbance in distant organs. The disease may be only functional at first, but, in time, induces organic lesions accompanied by atrophy. The organs which suffer most are the lungs, liver, kidneys, spleen, stomach, and brain.

The diseases following in the **lung** are chiefly *œdema and congestion*, *brown induration*, *pulmonary apoplexy*, *bronchitis*, and *acute croupous pneumonia*.

Pulmonary phthisis is almost unknown in a person who has been the subject of valvular disease. Valvular lesion, however, by no means infrequently constitutes a complication of pulmonary phthisis, the endocarditis which causes it sometimes being tubercular in its nature.

The **liver** is nearly always *congested*, and if the venous regurgitation should have been very great and sufficiently protracted, *cyanotic atrophy* of its substance follows. It is frequently *fatty*, but rarely, if ever, waxy. Waxy disease of an organ is almost, one might say, excluded if the individual suffer from valvular disease. Nor does it tend to become cirrhotic. The toughness of the typical "heart" liver is not due to excess of fibrous tissue.

The **kidneys** become greatly indurated and enlarged (*cyanotic induration*); the medulla is deeply congested, and the Malpighian bodies are rendered prominent from the same cause. Recent yellow embolic *infarctions* are common, and the depressed cicatrices left after their absorption, are even more so.

They are sometimes *cirrhotic*, but not often, and it is questionable whether the cirrhosis is due to the valvular defect; it is frequently the result of cicatricial contraction from old infarctions. The cirrhosis may, in some cases, be traced back to the agent which brought about the endocarditis.

The statistics as to the frequency of cirrhosis given by Dickinson and Barclay seem much too high.

The **spleen** becomes enlarged, extremely firm in texture, and so congested with venous blood as to have a deep purple or black colour when opened. The colour, shortly after the cut surface is exposed,

[1] This subject is more fully considered in Section 551.

changes to a scarlet. *Infarctions* are common, and so are the cicatrices from them.

The mucous membrane of the **stomach** and of the **small intestine** is frequently very much engorged, and in a state of acute or subacute catarrh. *Punctiform hæmorrhages* are often seen upon it.

The **brain** is sometimes shrunken, the veins filled with blood, and the subarachnoid space distended with liquid. This organ, however, suffers less from regurgitant pressure than any of the before-mentioned. *Sanguineous apoplexy* occasionally, although not so often as might be supposed, constitutes a complication. The cerebral arteries may be perfectly healthy when the heart or aorta is advanced in atheromatous disease. *Embolism*, as would naturally be expected, is common, especially as a sequel to *endocarditis verrucosa*.[1]

The **capillaries** are sometimes seen to beat rhythmically, and synchronously with the heart's pulsation. The best method of demonstrating the phenomenon (Brunton, No. 179, v. p. 15) is the following:—The finger nail is drawn once or twice up and down the middle of the forehead. A red streak is left, which undergoes variations in width and brightness with each beat of the heart, sometimes visible at a distance of from five to six feet or more. The cause of the phenomenon is the recoil of the pulse wave permitted by an insufficient aortic.

Other Causes of Insufficiency of the Valves besides Endocarditis.

537. **Congenital.**—The valves are sometimes insufficient from birth, owing to malformation. The tricuspid, when diseased, is said to be often congenitally so, but the other valves are equally liable to deformity from this cause.

From Rupture of a Cusp.—Instances of rupture of a cusp from great muscular strain have been, from time to time, recorded in individuals who previously did not exhibit any signs of endocarditis. It is, of course, common enough where the valve becomes partially ulcerated and thus weakened. A regurgitant murmur, sometimes musical in character, is heard immediately after the injury.

From Rupture of the Chordæ.—Improbable as it might at first sight appear to be, the chordæ have been repeatedly described as having been torn across. In one case reported by Kelly (No. 192, xx. 1869, p. 153), the whole of the chordæ attached to the mitral are said to have been ruptured. One cannot help feeling that some of these cases might be accounted for through careless examination of the heart, whereby some of the chordæ had been accidentally torn or otherwise divided. Many of the records, however, seem to be reliable, as blood was found precipitated on the torn ends.

In other instances, the rupture had been a result of an ulcerative

[1] The diseases above referred to are described in detail elsewhere.

endocarditis situated on the tendon. The accident is alleged to have occasioned insufficiency by allowing an eversion of the edge of the valve during systole.

From Failure of the Base Muscles to Contract.—Macalister (No. 6, 1882, ii. p. 821) alleges that this prevents the atrio-ventricular cusps from duly approximating, and hence might be a source of insufficiency. It may simply be of temporary duration.

Spasmodic Muscular Contraction.—Irregular and spasmodic contraction of the musculi papillares has been held to account for certain otherwise inexplicable so-called *dynamic murmurs* (Sect. 580). The theory is that the muscle pulls irregularly upon the cusps, and hence renders them incapable of completely closing.

Disease of the Muscle.—Where the fibre of the ventricle is impaired in structure, as in anæmia, fevers, etc., the atrio-ventricular orifices may be found to be incompetent.

Dilatation of Ventricles.—This is insisted upon by Balfour as being a fertile cause of mitral incompetency. The large size of the cavity is said to prevent the cusps being accurately applied to each other.

Malformation of the Valves.

538. The semi-lunar valves of the **aortic** and **pulmonary artery** orifices are sometimes redundant: as many as four or five have been counted. They may also be numerically reduced. Two is by no means an uncommon number.

The malformation may affect the cusps of both arteries simultaneously. When there are only two, they may be of equal size, and, in the case of the aorta, a coronary artery opens behind the centre of each. Those of the pulmonary artery need not necessarily be symmetrical when the aortic are so; the aperture may be closed by one large and by another small flap. There is sometimes an imperfect septum in the centre of the large cusp.

There may be three cusps, but these so united, as to constitute a continuous diaphragm-like valve with three pouches. In other cases, only two of the cusps may be adherent, the third free. Three cusps may also be present, but one more capacious than the other two. These malformations are mostly due to intra-uterine endocarditis. The dilatation of a single cusp is often the result of disease in extra-uterine life.

Peacock (No. 322, p. 3) regards a redundancy of the valves as a sign of under-development rather than of over-development. He supposes that each cusp is developed in two parts, which subsequently unite, and that it is the failure to complete this union which occasions the congenital defect.

These malformations are often found associated with malformations of other parts of the heart. They may cause incompetence or constriction of the respective orifices.

The cusps of the **tricuspid** are sometimes found blended together into a continuous funnel-shaped membrane. As formerly mentioned (p. 615), the three cusps are perfectly continuous in health. The valve is in reality a continuous funnel-shaped structure, and a less accentuation of the depressions in its margin, which apportion off the cusps, would bring about the above defect.

The mitral appears to be much less seldom deformed than either the aortic or pulmonary. There is always difficulty in distinguishing between intra- and extra-uterine deformity of this valve.

Literature on Malformations of Valves.—**Andrew** (Pulmonary): Trans. Path. Soc., xvi. 1865, p. 81. **Barié** (Rupture, experimental): Rev. de méd., 1881, ii. pp. 132, 308. **Barwell** (Aortic): Trans. Path. Soc., xiii. 1862, p. 63. **Bergmann**: Ueb. norm. u. anomal. Chordae tendineae u. d. Bedeutung f. d. Enstehung norm. u. abnorm. Herzgeräusche, 1870. **Burns** (Tricuspid): Brit. Med. Journ., 1860, i. p. 301. **Carroll** (Tricuspid): Med. Rec., N. Y., xv. 1879, p. 57. **Carter** (Pulmonary): Trans. Path. Soc., xxiv. 1873, p. 48. **Coats**: Glasg. Med. J., xv. 1881, p. 372. **Duckworth** (Pulmonary): Trans. Path. Soc., xvii. 1866, p. 113. **Ebstein** (Tricuspid): Arch. f. Anat. Physiol. u. wissen. Heilk., 1866, p. 238; Schmidt's Jahrb., cxxxvi. p. 238. **Greenfield** (Mitral): Trans. Path. Soc., xxvii. 1876, p. 128. **Jenner** (Pulmonary): Trans. Path. Soc., iii. 1851-2, p. 301; *Ibid.*, iv. 1852-3, p. 102. **Marxsen**: Ein seltener Fall von Anomalie d. Tricuspidalis, Kiel, 1886. **Norman** (Pulmonary): Brit. Med. Journ., 1878, ii. p. 960. **Peacock**: On Malformation of the Aortic Valves as a Cause of Disease, Edin., 1853; *also* (Aortic), Trans. Path. Soc., ix. 1857-8, p. 61; *also*, Lancet, 1859, i. p. 391; *also*, Trans. Path. Soc., xxx. 1879, p. 258; *Ibid.*, xxx. 1879, p. 277. **Struthers** (Aortic): Month. J. Med. Sc., xvii. 1853, p. 274. **Wilks** (Pulmonary): Trans. Path. Soc., x. 1858, p. 79.

Cardiac Thrombi.

539. The majority of clots which are found in the heart are of *post-mortem* origin. They are large yellow masses of fibrin, most commonly occupying the left chambers, and often extending into the pulmonary artery. In diseases of hyperinosis, such as **pneumonia,** they are particularly well formed, and extend into the small branches of the pulmonary artery.

In **leucocythæmia,** the clots have a grayish-yellow purulent aspect. In **pernicious anæmia,** they are very pale yellow in colour and soft in texture. In **pyæmic** and **septicæmic states of the body,** they usually have a green colour.

These can, however, be hardly regarded as thrombi, seeing there is good reason to believe that, in most cases, they are precipitated either during the agony or after death. It is, in fact, even questionable whether the clots found in the auricular appendages can be regarded in the majority of cases as being of *ante-mortem* origin. In all the above cases, the clot lies over an unabraded surface, and is easily detached.

In **malignant endocarditis,** following upon delivery or other septic cause, polypus-like clots (cardiac polypi) are often found attached to some part of the endocardium. In some cases they have a green colour, and are solid throughout; in others they contain a cyst-

like cavity, and are more or less rounded and lobulated. They occasionally present a fleshy aspect, and are partially organised, from the underlying tissues having been pushed into them. The endocardium which they overlie, will be found almost certainly abraded; and micro-organisms are present in abundance in the thrombus.

Dickinson (No. 192, xiii. 1862, p. 60) recorded a case where a thrombus-like mass was found closely adherent to the wall of the right ventricle and extending into the pulmonary artery. The committee appointed to examine it pronounced it to be **syphilitic.**

Literature on Cardiac Thrombosis.—**Bristowe**: Trans. Path. Soc. Lond., vii. 1855-6, p. 134; *Ibid.*, xiv. 1863, p. 71; *Ibid.*, xix. 1868, p. 90; *also* (Cardiac Concretions), Reynolds' Syst. Med., v. 1879, p. 105. **Crisp** (Sudden Death from): Trans. Path. Soc., xxiv. 1873, p. 46. **Cruveilhier** (Purulent): Anat. path. du corps hum., livr. 28, pl. iv. **Dickinson**: Trans. Path. Soc., xiii. 1862, p. 60. **Douglas**: Edin. Med. Journ., xiii. 1868, p. 908. **Ewart (J.)**: Lancet, 1883, i. p. 188. **Ewart (W.)**: Trans. Path. Soc., xxix. 1878, p. 52. **Ferraro**: Riv. clin. Bologna, vi. 1886, p. 801. **Fredault**: Archiv. gén. de méd., xiv. 1847, p. 63. **Goodridge**: Practitioner, xxx. 1883, p. 412. **Griswold**: Trans. Med. Soc. Penn., Phila., xii. 1878, pt. 1, p. 339. **Hayden**: Dub. Qu. Journ. Med. Sc., xxxviii. 1864, p. 440. **Jones**: Lancet, 1883, i. p. 52. **Lejard**: Progrès méd., x. 1882, p. 107. **Macdonald**: Lancet, 1883, i. p. 210. **Macnamara**: Lancet, 1879, ii. p. 7. **M'Kendrick**: Edin. Med. Journ., xv. 1869, p. 396. **Monard**: Considérations générales sur les concrétions sanguines, etc., 1867. **Parrot**: Arch. de Physiol. norm. et path., i. 1874, p. 538. **Peacock**: Adventitious Growths in Heart, Reynolds' Syst. Med., iv. 1877, p. 165. **Poullet**: Recherches sur les caillots du cœur, 1866. **Ribail**: Progres méd., xi. 1883, p. 1056. **Richardson (R.)**: Lancet, 1867, ii. p. 641. **Schmidt** (Concretion): Deut. med. Wochnschr., xii. 1886, p. 936. **Tait**: Lancet, 1882, ii. p. 1004. **Thornton**: Lancet, 1883, i. p. 38. **Vadi**: De la mort rapide par thrombose cardiaque dans le rheumatisme articulaire aigu, 1874. **Vergely and Ferrier**: Journ. de méd. de Bordeaux, xiii. 1883-4, p. 290.

Effects of Chronic Disease of Particular Orifices upon the Size of the Others.

540. The general impression is that chronic disease of one or more orifices, in course of time, has a detrimental influence upon the size and competency of the others. Balfour (No. 289, p. 181), for instance, holds that the most frequent cause of serious tricuspid regurgitation is mitral stenosis, but that great obstruction at the aortic orifice may have a similar effect. The blood, in the former case, is hindered in its passage onwards, and hence tends to regurgitate upon the right side of the heart. On the other hand, aortic regurgitation, although a frequent enough disease, is anticipated in its injurious results on the other orifices by its own peculiar sources of mortality, and hence it is only comparatively rarely that aortic regurgitation gives rise to serious tricuspid regurgitation. The following results derived from the author's own observations show, among other things, that the incompetence of the unaffected valves, if incompetence there be, is not caused in the majority of cases by dilatation.[1]

[1] The same means of measurement were adopted, and the statistics were derived from the *post-mortem* records through the same number of years, as in the case of normal hearts. (Chap. XXXVII.)

(A) Pure Aortic.

(1) *Aortic of Normal Size but Incompetent.*

541. In this case, the average size of the various orifices was the following :—

Aortic	Mitral	Pulm. Artery	Tricuspid
·99 in.	1·3 in.	1·1 in.	1·8 in.

On comparing this with the normal measurements given at p. 579, it would thus seem that in simple regurgitant aortic without alteration in the size of the orifice, the effect upon the size of the other orifices is practically *nil*.

(2) *Aortic Constricted and Incompetent.*

Aortic	Mitral	Pulm. Artery	Tricuspid
·75 in.	1·3 in.	1·1 in.	1·7 in.

Here the result is very much as in the foregoing, the effect upon the tricuspid being even less than in it.

(3) *Aortic Dilated and Incompetent.*

Aortic	Mitral	Pulm. Artery	Tricuspid
1·2 in.	1·7 in.	1·2 in.	2 in.

The result is different from that in the two foregoing. As will be noticed, the effect of the dilated and incompetent aortic has been to *induce a general distension of all the other orifices.* The explanation simply is, that the wide incompetent aortic allows of a sudden and full regurgitation of the arterial blood upon the left ventricle during diastole, that is to say, while the mitral valve is open. This diastolic reflux, continued for a sufficiently long time, induces a widening of all the other orifices, from the constant state of distension in which the pulmonary artery and the right chambers of the heart are retained. The more constricted the aortic becomes, the less will this direct regurgitant arterial pressure be felt by the sound orifices.[1]

The records did not show a single case in which the aortic, when alone diseased, was constricted without being incompetent. The incompetency was, however, sometimes slight.

(B) Pure Mitral.

(1) *Mitral Constricted and Incompetent.*

542. The evil effect of this, which is the commonest lesion of the mitral, upon the size of the other orifices is inappreciable, as the accompanying figures testify :—

[1] The mechanism of the arterial recoil is explained more fully in Section 551.

Aortic	Mitral	Pulm. Artery	Tricuspid
·97 in.	·86 in.	1·1 in.	1·7 in.

This result is probably to be explained by the constriction in a manner modifying the distending influence of the mitral regurgitance upon the orifices of the right side.

(2) *Pure Dilatation of the Mitral.*

543. A dilatation of the mitral, with a competent and otherwise healthy aortic, comes to pass very seldom. The author's total records of the examination of the heart in persons dying from all manner of diseases show only seven examples of this lesion. A congenitally large mitral, with corresponding enlargement of all the other orifices, occurred in eleven instances. In only one case of mitral dilatation was there evidence of endocarditis, and, in this single example, it was of an acute nature and of septic origin. In none of them was it noted that a murmur was audible, although, from the necessarily brief record of the history in the *post-mortem* journals, too much reliance should not be placed upon this statement.

Passing over in the meantime those which were evidently congenital enlargements, or, at least, in which the orifices were all equally dilated, let us examine the effect of the dilatation of the mitral upon the other orifices. The figures are the following :—

Aortic	Mitral	Pulm. Artery	Tricuspid
1 in.	1·68 in.	1·27 in.	1·98 in.

This practically shows that with a mitral of 1·7 in. diameter the pulmonary artery and tricuspid corresponded respectively to close on 1·3 and to 2 in.

Most of the subjects unfortunately died from lung disease, and hence it is difficult to say in how far the dilatation of the right orifices was due to this cause. It should be mentioned, however, as supporting the belief that the dilated mitral, in reality, was one of the chief factors in inducing the enlargement, that the dilatation of the right orifices was quite as great in those cases where the lungs were sound, or, at any rate, in which they were not the seat of disease unconnected with the cardiac condition.

(C) Aortic and Mitral Combined.

(1) *Aortic and Mitral both Constricted, Aortic Competent, Mitral Incompetent.*

544. It might be expected that the orifices on the right side would suffer dilatation. Such, however, as will be seen from the accompanying results, was not the case.

Aortic	Mitral	Pulm. Artery	Tricuspid
·7 in.	1 in.	1·1 in.	1·6 in.

It is probable that the constriction of the mitral in this, as under other circumstances, prevented the deleterious effects of the regurgitance through its orifice being felt.

(2) *Aortic and Mitral both Constricted and both Incompetent.*

545. The measurements were the following :—

Aortic	Mitral	Pulm. Artery	Tricuspid
·8 in.	·77 in.	1·08 in.	1·6 in.

The only effect upon the orifices of the right side, be it a consequence or a mere coincidence, was that of rendering them, if anything, actually somewhat smaller than those of the average healthy heart, more especially as this class was entirely taken from males.

(3) *Aortic of Natural Size but Incompetent, Mitral Constricted and Incompetent.*

546. Nearly 50 per cent of the cases were females, and, as will be seen, the effect upon the size of the orifices of the right side was inappreciable.

Aortic	Mitral	Pulm. Artery	Tricuspid.
·97 in.	·87 in.	1·1 in.	1·6 in.

(D) Tricuspid.

547. The cases of tricuspid disease which came under the author's notice were unfortunately all combined with disease of the left orifices, and hence no differential conclusions could be drawn from them.

SUMMARY OF THE FOREGOING RESULTS.

548. The preceding data lead up to the somewhat remarkable conclusion, that the only lesions of the left side which are accompanied by any appreciable distension of the otherwise sound orifices are uncomplicated aortic regurgitance with a wide orifice, and uncomplicated dilatation of the mitral. In the former of these, the three remaining orifices were considerably above the average diameter, and in the latter, both the pulmonary artery and tricuspid were distended, while the aortic remained of natural size. As regards the other classes, it may be noted that, where incompetence of a valve was accompanied by constriction of the orifice, the remaining apertures were not sensibly affected. The legitimate conclusion to draw from this result appears to be that, so far as the distension of the other orifices of the organ is in question, constriction of an incompetent orifice exerts a salutary influence upon them.

On referring to p. 641, it will be found that constricted aortic and mitral, where both are incompetent, occasion great hypertrophy of the right ventricle, whereas we have just seen that this lesion has but little influence upon the size of the right orifices. At first sight, this result seems somewhat at variance with what might be expected, but it may probably be explained in the following manner :—The constricted aortic and mitral will prevent such a direct recoil of the arterial blood during diastole as would happen were they of natural size or dilated. This will tend to keep up a chronic state of high tension within the pulmonary circuit, rather than to subject it to sudden exacerbations of pressure. Such a continuous strain, without the orifices becoming much enlarged, in course of time will induce hypertrophy of the right ventricle, seeing that it will have to contract more energetically in order to open the pulmonary artery valve. Where, however, the aortic and mitral openings are wide, and where the aortic is incompetent, there must, in addition, be an instantaneous recoil of the arterial pressure upon the whole pulmonary system during each diastole, with a sudden stretching of the orifices. The result most probably will be that both distension of the right orifices and hyptertrophy of the wall of the right ventricle will follow.

CHAPTER XLI

THE HEART—(*Continued*)

Hypertrophy and Dilatation

549. The pathology of hypertrophy is so intimately bound up with that of dilatation, that it is practically impossible to treat of them separately. They are, of course, frequently, although not always, combined.

GENERAL CAUSES OF HYPERTROPHY.

These may be divided into two great classes, namely, (1) where the hypertrophy is caused by valvular disease; and (2) where no such complication is present, but where disease of the kidneys, or of other distant organ, or some constitutional affection, has preceded it.

ANATOMICAL DESCRIPTION OF THE HYPERTROPHIED HEART.

The heart is both elongated and increased in breadth. The elongation, however, is perhaps the more constant feature of the two. It exposes a greater surface anteriorly than when the organ is of natural size. The walls of the ventricles are more often the subject of it than those of the auricles. It may sometimes be so large as to resemble the heart of an ox (bukardia). It is rare that one ventricle is hypertrophied without the other to some extent participating, although disproportionately so.

Along with an hypertrophied wall, the cavity may be of normal size, dilated, or contracted. The terms **simple, eccentric**, and **concentric hypertrophy** are respectively applied to the organ under these circumstances.

The usual thickness of the normal left ventricle is about $\frac{1}{4}$ in. at its apex, and $\frac{1}{2}$ in. at its base. In extreme hypertrophy it may reach from $\frac{1}{2}$ to $\frac{3}{4}$ in. at the apex, to $1\frac{1}{4}$ or $1\frac{1}{2}$ in. at the base.

The muscular fibre is, as a rule, well nourished, hard, and of a dull

pinkish-gray colour when first incised, becoming bright red on exposure. The musculi papillares and columnæ carneæ generally participate in the enlargement.

It is probable that the increase in fibre is chiefly numerical. Zielonko (No. 13, lxii. 1874, p. 29) was led to this conclusion from the study of hypertrophy of the frog's heart, the result of partial ligature of the aorta.

In the heart of the frog the majority of the fibres are branched or spindle-shaped, and highly nucleated. Between these, however, are more or less rounded or obtusely spindle-shaped bodies. They represent the young muscular elements, and, so far as known, are the result of division of pre-existing muscular fibres.

These increase largely during the time that the hypertrophy is proceeding, and, in their turn, become muscular fibres.

Hepp's researches (No. 304, quoted by Schroetter) would, however, tend to show that there may also be a slight increase in their size. Taking 0·007 mm. as the diameter of the normal human fibre, he finds that in hypertrophy it may come up to 0·03 mm.

The nerves were said by Lee (No. 305) to be thickened in the hypertrophied heart; and Cloetta (No. 13, v. 1853, p. 274) stated that he had confirmed this. It may, however, be justly doubted whether such is of invariable or even frequent occurrence.

Hypertrophy and Dilatation from Valvular Disease.

(A) Aortic.

550. Although, in the majority of aortic lesions, hypertrophy of the left ventricle will be found to co-exist, yet, as Gairdner (No. 148, xxiii. 1853, p. 211) remarks, there is a capriciousness as to its presence or absence, which is hard to explain. When the aortic is experimentally injured, the reserve energy of the ventricle, which, as shown by Rosenbach (No. 104, ix. 1878, p. 10), is considerable, is called forth. It contracts more energetically, and does so until new muscular fibre is generated in sufficient amount to compensate for the defect. Dilatation ensues in course of time, and is followed by hypertrophy (*loc. cit.*, p. 12). Balfour states (No. 289, 1876, p. 71) that such is also the sequence of events in Man.

Why does dilatation take place, and what is the increased work performed by the heart, calling forth the hypertrophy of its fibre?

Let us consider the simplest aortic lesion to begin with, namely,

(1) *AORTIC INCOMPETENCE WITHOUT CONSTRICTION OR DILATATION OF THE ORIFICE, THE MITRAL BEING NORMAL.*

551. The primary and immediate result here, of course, will be to cause the blood to regurgitate from the aorta during ventricular diastole, so that the cavity is filled from two sources instead of from one. Increased strain will be thrown upon the cardiac muscle from

the arterial recoil, and there will be a much greater tendency to dilatation than in health.

Arterial Recoil.—The blood in a sound heart flows passively into the ventricle, at least during the first stage of diastole, without receiving much, if any, impulse from the auricle. The latter contracts as it is becoming emptied, and drives the remainder of the blood out of its cavity. The blood must therefore impinge against the ventricular wall with very little force during health, and hence the strain will be comparatively slight. It has even been said by Pettigrew (No. 78, p. 115) that the dilatation of the ventricle is a vital act.

In simple aortic regurgitation, however, the arterial recoil must be enormous, and it occurs during diastole. Rosenbach (*loc. cit.*, p. 14) found it to be sufficient to induce aneurism of the apex in animals in which the valve had been artificially destroyed.

Cause of Arterial Recoil.—The cause of the recoil is usually held to be the elasticity of the arterial walls. It is, however, doubtless erroneous to regard this as the only cause. In estimating the factors which are instrumental in raising the blood pressure, the arteries are commonly looked upon, as if they were a series of exposed tubes. In reality, however, there is no part of the body in which the arteries and capillaries can be said to be exposed. The nearest approach to it is in the case of the capillaries on the alveolar walls of the lung; but even here, they are connected to an eminently elastic tissue, and are covered by epithelium. In all other parts, they are bound down by tissues, more or less resilient (yellow elastic fibre, white fibrous tissue, muscle, etc.), whose interspaces are filled with liquid. This liquid will consequently tend to diffuse the elastic pressure of the tissues, and to bind it to that of the arterial wall. Even in the abdomen, the tissues are all so intimately and mutually contiguous that the so-called abdominal cavity may be regarded as non-existent. Finally, the skin and the immediately subjacent tissues are so elastic that they tend to complete a counterpoise sufficiently strong to resist the expansile efforts of the heart transmitted throughout the whole body by the hydraulic machinery of the blood-vessels.

Donders (No. 144, i. p. 172) seems to have been the first to draw attention to this relationship of the arterial walls to the tissues encompassing them. He says: "We have previously seen that the blood-vessels do not bear the entire blood-pressure. They would become more expanded if they were not supported by the surrounding tissues. Part of the blood pressure is expended upon the tissues and the nutritive liquids which bathe them."

Some years since, the author endeavoured (No. 5, xiii. 1879, p. 518; also No. 19, xxvii. 1881, p. 385) to demonstrate the importance of the influence exerted by this elastic reaction of the tissues on the processes of healing and organisation.

Landerer (No. 113, 1884) has lately gone fully into the matter, and has based certain theories of dropsy and inflammation upon it.

There cannot be much doubt, that the subject of the relationship of the elasticity of the tissues and of their contained liquids to the cir-

culating blood is one of the most profound in all pathology, and is one which has hitherto been much disregarded. We have been in the habit of attributing variations in the elasticity of the arteries exclusively to modifications of the arterial wall. It must, however, be sufficiently ostensible, on reflection, that as the arterial and capillary coats and the surrounding tissues and liquids may practically be regarded as continuous and as constituting one texture, any modification in the elasticity of the fibre of the latter, or any difference in the quantity of liquid lying in the interspaces, must react upon the blood in the vessels in very much the same manner as the arterial wall itself.

During muscular exertion, moreover, the pressure of these liquids will be increased, and will constitute at least one of the factors which will go to raise the arterial tension and augment the aortic recoil.

Effect on Ventricle.—All such exacerbations of pressure have to be borne by the ventricular wall, the mitral orifice, the lung, and the right side of the heart; and the larger the aperture of the aorta, as previously pointed out, the more suddenly will the returning gush of blood impinge upon them, and the greater will its influence for evil consequently prove. The mitral orifice and the orifices on the right side, as already demonstrated, will accordingly become unnaturally large, and the ventricles will also increase in capacity.

The dilatation of the ventricle would no doubt continue to be progressive, were means not forthcoming to withstand the undue backward strain brought to bear upon its interior.

Counteraction in Hypertrophy.—The provision against this unlimited dilatation is to be sought *in the hypertrophy of the muscular fibre.* The mass of new muscle maintains the *tone* of the heart, like that of the arteries in cirrhotic Bright's disease or other chronic affection accompanied by a high arterial pressure.

Tonic Function of Heart.—The muscle of the heart, like involuntary muscle surrounding other cavities, has a twofold action. It drives out the contents of the cavity and it prevents over distension.

It is otherwise difficult to explain how the heart, even in health, with the constant filling of its cavities, does not in time become distended. The heart muscle thus seems naturally to possess a tonic function analogous to that of the musculature of the arteries, and this is brought more especially into play when the aortic blood is allowed, through insufficiency of the valve, to recoil upon the interior of the ventricle during diastole.

This tonic function of the heart muscle is often overlooked, but must be one of very considerable importance.

Gaskell (No. 179, iv. pp. 116-118), in summing up the results of his admirable paper on the innervation of the heart, concludes that muscular tissues exhibit three modes of responding to stimulation. Certain muscles possess essentially the power of "tonic contraction," others the power of "rhythmical contraction," and others that of "rapid contraction."

The *striated muscle of vertebrates* is characterised by—
Rapidity of contraction being most highly developed ;
Tonicity rudimentary ; and
Rhythmic action still more rudimentary.
Cardiac muscle by—
Rhythmic action being most highly developed ;
Rapidity of contraction well marked ; and
Tonicity well marked.
Unstriped muscle by—
Tonicity being most highly developed ;
Rhythmic action well marked ; and
Rapidity of contraction most rudimentary.

The ventricle probably meets the increased strain to which it is subjected in aortic regurgitant disease by being thrown into a series of small contractions before the true systole commences, hence possibly the jar sometimes communicated to the finger by the pulse in this form of valvular disease.

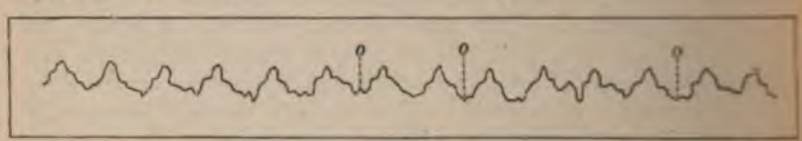

FIG. 195.—TRACING FROM CAROTID IN AORTIC REGURGITATION, SHOWING NUMEROUS SECONDARY WAVES.

Marey (No. 346, p. 679) gives a curious tracing (Fig. 195) from the carotid artery of a person who suffered from aortic insufficiency, in which numbers of small secondary waves are seen in the diastolic part of the sphygmogram and during the period of rest preceding the ventricular contraction. He interprets these as a consequence of contraction of the auricle. The phenomenon, however, might be explained by the suddenly injected aortic blood impinging upon the wall of the ventricle and throwing the latter into a series of spasmodic contractions of minor import before the true ventricular systole commenced.

Tonic Function of other Visceral Muscles.—It is indeed probable that the muscular fibre which surrounds any hollow viscus in the body subserves the purpose of maintaining the tone of the organ, and of thus preventing over-distension of its cavity. The muscular fibre of the arteries hypertrophies when unduly great distensile strain is put upon the arterial walls, so does that of the bronchi and of the bladder, and it is only reasonable to suppose that the heart muscle hypertrophies under like circumstances.

Further Overwork of Ventricle.—Such being one of the sources of overwork to be performed by the heart in the lesion we are at present contemplating, let us next consider what further sources of strain, if any, it has to contend against.

In health, the pressure of the blood during systole has to rise

superior to that of the blood in the aorta before the aortic valve will open. If the valve is destroyed, and if the orifice be of natural calibre, will the intraventricular pressure have to reach a higher pitch before the blood will leave it to pass into the aorta? Obviously not, for the arterial pressure, there is good reason to believe, remains the same as before. The function of the valve is only called into play during the diastole of the ventricle; it is in abeyance, and might as well be absent during systole.

Rosenbach (No. 104, ix. 1878, p. 1), employing dogs and rabbits, found that extensive destruction of the aortic, mitral, or tricuspid had no material effect in altering the arterial blood pressure. In rabbits which were allowed to live for different periods after the valves were rendered incompetent, the arterial pressure was still uninfluenced. If, moreover, the orifice of the aorta was narrowed by the introduction of a sound, still no effect followed.

De Jager (No. 49, 1883, ii. p. 142) obtained the same results, in dogs, after insufficiency of the aortic, mitral, or tricuspid had been artificially induced, but, in rabbits, an absolute fall in the arterial pressure was noticed.

The ventricle, in uncomplicated aortic regurgitance, will, therefore, not have to work unduly hard, in order to compensate for increased arterial resistance.

It might possibly act at a disadvantage during systole were the cavity dilated, seeing that a greater mass of blood would have to be propelled forwards than in health. On the contrary, were the cavity not increased in size, the overwork thrown upon the heart would chiefly be that of resisting arterial recoil when the ventricle is dilating and of so maintaining the tone of the organ.

Conclusion.—*The recoil of the arterial blood upon the interior of the ventricle is one of the main obstacles to be overcome in uncomplicated aortic regurgitance, and constitutes the chief, if not the only, increased work to be done.*

(2) *AORTIC INCOMPETENCE WITH A DILATED ORIFICE, MITRAL NORMAL.*

552. Here the conditions are simply an exaggeration of those in the preceding. From the fact that the wide orifice will permit of a less impeded arterial recoil, the impulse communicated to the interior of the ventricle by the sudden reflux of blood will be more sudden than in the former, and hence the strain during the commencement of diastole will be greater. There will be, if anything, however, less difficulty in propelling the blood through the widened orifice during systole than before, and hence increase of *propelling power* of the ventricle would be called for, only where the cavity was much dilated.

As a matter of fact, the author's statistics show that the cavities of the ventricles are not so large as in the foregoing class ($3\frac{3}{4}$ in. for each side as compared with 4 in. for the left and $4\frac{1}{4}$ for the right), but that the ventricular wall is thicker. It may possibly be that the wide aortic

orifice throws so great a strain upon the ventricle that the muscle hypertrophies before dilatation has reached so high a pitch.

Conclusion.—*The chief overwork performed by the heart in aortic regurgitation with a wide orifice is in keeping up the tone of the ventricle.*

(3) *AORTIC REGURGITANCE WITH A CONSTRICTED ORIFICE, MITRAL NORMAL.*

553. The effect of constriction, over and above the incompetence, will be twofold. It will lessen the arterial recoil, or, at any rate, will permit of the blood regurgitating less suddenly than where the orifice is wide, and at the same time it will tend, by narrowing the outlet, to render the difficulty of propelling the blood forwards during systole greater.

By the former, the shock communicated to the interior of the ventricle will be less than where the orifice is wide, and hence, probably, the hypertrophy ought not to be so great as in either of the other preceding forms.

As will be seen from the following tabulated statement of the effects of aortic disease on the wall (p. 635), this is borne out in fact. The constriction of the orifice will thus in a manner compensate for the regurgitation, and diminish the hypertrophy or dilatation which would otherwise follow.

The constriction, on the other hand, will hinder the blood from passing out of the ventricle, and will therefore reflect its influence upon the wall. If the ventricle empties itself, it is clear that pure aortic constriction never could cause a dilatation. If a distended hollow viscus be compressed on all sides from without inwards, it will never become dilated. It is during the diastole that dilatation alone can be effected, the pressure then being from within outwards.

Of course, it might be urged that the ventricle empties itself incompletely at each systole, and that the blood tends to accumulate within it. This is, however, mere theory, and may well be called in question. If blood tends to accumulate in a chamber of the heart, where does the accumulation end?

The hypertrophy in this lesion should, therefore, probably be traced, firstly to the arterial blood regurgitating during diastole, and, secondly, to the increased efforts required to be put forth by the heart wall during systole. The effect of the regurgitance, however, will be modified by the constriction, and hence will be less injurious than where the orifice is full sized or dilated. The sum of the effects of both agents might come to be very much the same, in regard to the condition of the wall, as the single effect of a dilated incompetent orifice or one of natural size.

Conclusion.—*The overwork performed by the heart, where the aortic is incompetent and constricted, is twofold, namely,* (1) *that of keeping up the tone of the ventricle, and* (2) *that of driving the blood through a narrow orifice.*

COMPARATIVE EFFECTS OF THE FOREGOING THREE FORMS OF AORTIC DISEASE UPON THE VENTRICULAR WALLS AND CAVITIES.

554. The above three forms of disease of the aortic constitute by far the largest proportion of pure aortic cases. As previously mentioned (p. 624), the author has failed to find in his records a single instance of simple constricted aortic without the valve being, after death, incompetent, although sometimes only slightly so.

The following table gives a connected view of the influence exerted by the three forms of aortic disease just referred to upon the walls and cavities of the ventricles.

	Ventricles.		Walls (maximum thickness).	
	Left.	Right.	Left.	Right.
1. Aortic of normal diam. and incompetent	4 in.	$4\frac{1}{2}$ in.	$\frac{5}{8}$ in.	$+\frac{3}{16}$ in.
2. Aortic constricted and incompetent .	$3\frac{1}{2}$,,	$3\frac{1}{2}$,,	$\frac{3}{8}$,,	$+\frac{1}{8}$,,
3. Aortic dilated and incompetent . .	$3\frac{3}{4}$,,	$3\frac{3}{4}$,,	$+\frac{3}{4}$,,	$+\frac{1}{4}$,,

It would thus appear that, where the orifice was of natural size, the left ventricle was largest; that it was of medium capacity, where the orifice was dilated; and that it was smallest where the orifice was constricted.

The thickness of the wall, however, it will be noticed, was greatest where the orifice was largest, least where it was of natural size or constricted. This is exactly what would be expected, reasoning on the data before mentioned. The greatest arterial recoil takes place with the dilated aortic, the least with the constricted. In the case of the constricted, however, the impediment to the propulsion of the blood constitutes an additional cause of hypertrophy, and hence there is good reason for the wall being as thick as the figures show it to be.

We have previously seen that the dilated aortic regurgitant also exerts the most injurious distensile effect upon the other orifices, and there is little doubt that this form of valvular disease is one of the most disastrous to which a heart can be subjected. The more suddenly the defect is brought about the greater the danger. It is accompanied to a larger extent than any other cardiac lesion by the evils which follow in the train of free regurgitant arterial pressure applied during diastole.

COEXISTENT DILATATION OF RIGHT VENTRICLE.

555. Gairdner, a good many years ago, remarked (No. 148, 1853, p. 218) "that he had never seen an instance of hypertrophy affecting the left side alone." In spite of what less accurate observers fre-

quently assert to the contrary, there is much truth in this statement. And not only does it hold good of hypertrophy of the ventricular walls, but may with almost equal force be applied to dilatation of their cavities.

From the foregoing statistics of aortic disease, it will be noticed that the size of the right ventricle had advanced almost *pari passu* with that of the left, and indeed, in one case, had over-reached it. There was also a certain correspondence in the thickness of the wall of the right ventricle as compared with that of the left.

The coincidence of a dilated and hypertrophied state of the right ventricle with a similar condition of the left is perhaps to be accounted for by the regurgitant arterial pressure on the left side influencing the whole of the mechanism of the right.

CAUSE OF HYPERTROPHY OF MUSCULI PAPILLARES.

The musculi papillares probably act as a stay upon the valve to which they are attached, and thus prevent eversion during systole.

Pettigrew (No. 78, pp. 278, 280) describes the cusps of the mitral as being floated up during the ventricular diastole. During systole, however, the blood is thrown by the action of the ventricle into spiral columns, and twists them into each other while the musculi papillares drag them downwards.

Sée (No. 4, i. 1874, p. 552) believes that the papillary muscles contract at the same time as the ventricle. They tighten the chordæ and pull the cusps down. The left cusp of the mitral plays much the more active part in closure, but the right is not unemployed.

The musculi might, accordingly, be expected to hypertrophy where the aortic orifice is constricted, for here the increased effort required to propel the blood through the orifice would also react upon the mitral cusps, and tend to force them upwards.

EFFECT OF FILLING OF THE LEFT VENTRICLE FROM TWO SOURCES.

556. As the left ventricle is filled both from the aorta and from the auricle in aortic regurgitation, it follows that there must be a mixing of the blood from the two sources of supply within the chamber. The gross effect will be, of course, to lessen the amount of ærated blood passing from the lungs into the aorta and systemic arteries.

The proportion in which the auricular and aortic bloods mix is an interesting and as yet undetermined question. The proportional pressure within the pulmonary artery, as compared with that of the aorta, has been variously estimated at 2 : 5 or 1 : 3. The pressure within the pulmonary veins is considerably less, while that within the auricle, at least towards the end of auricular systole, is again somewhat increased but still considerably below the pressure of the blood within

the aorta. The result must therefore be, that more blood will regurgitate from the aorta than will pass into the ventricle through the auriculo-ventricular opening. The auriculo-ventricular opening, however, is larger than the aortic, and hence there might be less obstacle to the free passage of the auricular blood than to the regurgitation of the systemic.

PREVENTION OF RECOIL UPON THE LUNG.

557. The pulmonary veins are without valves, and the regurgitation from the aorta occurs during diastole, hence at a time when the auriculo-ventricular orifice is open. It might *a priori* be expected that if the pressure within the aorta be greater than that in the auricle, its injurious influence would be brought to bear directly upon the lung. Such is often the case, but not always. It is a well known fact that individuals with aortic disease frequently know nothing of it until they are examined for life insurance or for some other reason.

The absence of injurious effects might be accounted for by the pulmonary veins rhythmically closing as the auricle begins to contract. If some provision of this kind were not present, it is difficult to see how the circulation could continue for any length of time.

If the orifices of these vessels do close, then it is possible to conceive that the hypertrophied ventricle keeps up the tone, and that, with each systole, a blood composed say of two parts aortic and one part auricular is propelled forwards.

This might naturally be supposed to occasion such an under-oxygenation of the blood that the system would materially suffer, and it does so in certain cases. It must be remembered, however, that if the blood be delayed in its passage through the lung, provided the bronchi and air-vesicles are unobstructed, it becomes *hyperoxygenated*. Hence, although the fresh blood from the lung circulates less freely, yet its hæmoglobin may contain so much oxygen as in a manner to compensate for the defect.

If, moveover, the auricle were to hypertrophy, the blood would be driven into the dilating ventricle with impetus sufficient, in a manner, to equalise or exceed that caused by the arterial recoil.

Landois (No. 32, i. p. 80) remarks that hypertrophy of the left auricle occurs as a result of aortic insufficiency "because the auricle has to overcome the continual aortic pressure within the ventricle." As a matter of fact, it will be found that hypertrophy of the wall of the left auricle in this disease is not of common occurrence, but that the cavity, as a rule, is slightly dilated. The dilatation is not so extensive, however, as when the aortic regurgitance is complicated with mitral incompetence and stenosis, for, under these circumstances, the forces tending to dilate the auricle are of a threefold nature. In the first place, there is the arterial recoil during ventricular diastole; in the second, the hindrance to the free passage of blood from the auricle into the ventricle, owing to the constriction of the auriculo-ventricular orifice, also occurring during diastole; and in the third, the

regurgitant systolic impetus conveyed to the auricle during systole. The auricle in this form of disease will be found to be larger than in any other, while in pure mitral disease it is usually of medium capacity.

Hypertrophy of the auricles does not follow lesion of the orifices with the same facility as that of the ventricles. Hence the abnormal conditions of pressure arising from valvular disease will be found to leave their record oftener in auricular dilatation than in an increased thickness of wall.

(B) Mitral.

(1) *MITRAL INCOMPETENCE WITH STENOSIS, AORTIC NORMAL.*

558. In this, which is the usual form of mitral disease, it might theoretically be expected that the tendency to hypertrophy and dilatation of the left ventricle would be less than in aortic incompetence. There is no arterial rebound upon the ventricular wall during diastole, and from the narrowing of the mitral orifice the blood will be impeded in its flow from the auricle, and hence might not reach the ventricle, even with such force as is imparted to it in health.

There is, however, a cause for hypertrophy in this case which is absent in simple aortic disease. The incompetent mitral allows part of the ventricular blood to recoil during systole upon the left auricle, and this will naturally tend to weaken the impulse communicated to the systemic vessels. The ventricle will thus have to work harder in order to keep up the arterial pressure.

Artificial destruction of the mitral in an otherwise healthy animal, as before remarked, does not cause a fall in arterial blood pressure, probably from the ventricle contracting more vigorously, and from the openings of the pulmonary veins closing sufficiently to limit the regurgitant effects to the auricle.

It is very unlikely, however, that the orifices of these vessels would withstand the dilating influence of this regurgitance for long. There is every probability that, if the thin wall of the auricle became dilated, they would also widen, and thus allow of the influence of the ventricular systole being felt by the whole pulmonary circulation as far back as the pulmonary artery orifice.

The result ought to be, as the following figures show is the case, that this lesion of the mitral induces slight hypertrophy of the wall of the left ventricle.

	Ventricles.		Walls (Maximum Thickness).	
	Left.	Right.	Left.	Right.
Mitral constricted and incompetent	+3¼ in.	+3½ in.	⅛ in.	⅛ in.

Rosenstein (No. 206, vi. p. 126), remarks that, in this valvular defect, the left ventricle is so small as compared with the dilated right, that it looks almost like an appendage of the latter. The above figures do

not entirely support this statement. The difference in the dilatation of the two cavities, as will be noticed, was comparatively slight, and there was no appreciable hypertrophy of the right.

(2) *MITRAL DILATED, AORTIC NORMAL.*

559. This being a rare condition, and not always accompanied by regurgitation, it is difficult to say what its actual effects might be. The large mitral, of course, if incompetent, would allow a still greater reflux than in the foregoing. The combination of a dilated mitral orifice with any amount of incompetency, must, however, be looked upon somewhat in the light of a pathological curiosity.

The following figures may be taken for what they are worth :—

	Ventricles.		Walls (Maximum Thickness).	
	Left.	Right.	Left.	Right.
Mitral dilated, but doubtful whether incompetent .	3¾ in.	4 in.	+ ½ in.	$\frac{3}{16}$ in.

(3) *MITRAL CONSTRICTED AND COMPETENT, AORTIC NORMAL.*

560. This, as previously indicated, is also a rare lesion. The commonest cause of it is the projection into the funnel-shaped valve of vegetation or calcareous masses, tumours, etc. In other instances, the margin of the valve is alone contracted without the valve being converted into a leather-like structure, a condition which apparently is compatible with the valve closing.

The effects of such a lesion, of course, would be to hinder the blood in its transit from the auricle to the ventricle, unless the auricle compensatorily hypertrophied to drive it onwards with increased force.

(C) Aortic and Mitral combined.

(1) *AORTIC AND MITRAL BOTH CONSTRICTED AND BOTH INCOMPETENT.*

561. The heart under these conditions may be regarded as a rhythmically contracting tube unprovided with competent valves at either end. The systemic arterial supply thus becomes directly continuous with the pulmonary. They form one set of vessels with this rhythmically contracting chamber, the mutilated auricle and ventricle between them. The scheme of the circulation in fact comes to resemble that of the fish. There is one auricle and one ventricle (the right), with a vessel (pulmonary artery) conducting to the lungs, vessels

conveying the blood (pulmonary veins) to a pulsatile vessel or chamber (the left auricle and ventricle), thence to the systemic arteries.

Effect.—The ultimate result must of course be, that, during ventricular diastole, the pressure within the pulmonary vessels, as far back as the nearest obstruction, *i.e.* the pulmonary artery orifice will tend to be equalised with that in the systemic arteries. In fact, if the mitral fails to close, and if its aperture, although narrow, remains larger than the constricted aortic, as usually happens, the ventricular blood ought by preference to pass backwards through the mitral instead of forwards into the aorta. The lung would thus have imparted to its vessels actually more of the ventricular energy than is exercised upon the systemic arteries, the only counterbalancing agent being the pulmonary blood which is being driven in the opposite direction by the right ventricle.

The **Pulmonary Capillaries** would, moreover, have to bear, at each ventricular systole, both the pressure imparted to them by the right ventricle, and that due to regurgitation. They are not even free from injurious over-pressure during ventricular diastole, because they are then subject to the backward recoil of the whole arterial system.

It cannot be a matter of wonder that, under the circumstances, the delicate-walled capillaries of the lung, entirely unsupported as they are on one side, should become converted into huge nævus-like masses. They, in fact, have to support from three to five times the pressure they were originally intended to bear, and it is only because they are so elastic that the effects of this do not prove to be more disastrous than they are.

Limit of Regurgitance.—But where does this regurgitant effect cease? Theoretically, it ought not to be felt beyond the next lock, that is to say, beyond the orifice of the pulmonary artery, provided that the valve of this vessel remains competent. The orifice is very rarely altered in size, and incompetency of the cusps is a thing almost unknown. The sharpness with which they can be heard to click together in such a case is evidence of their timely and often premature closure. How do the organs on the right side of the heart therefore come to suffer?

We have seen (p. 626) that, in the majority of valvular lesions of the left side, the tricuspid and pulmonary artery orifices are not altered in diameter. It might, accordingly, well be argued that, so long as the pulmonary artery orifice is competent, this regurgitant pressure imparted to the lung could not possibly affect the organs further back. Yet pulsation may be felt and seen in the jugulars and in the liver in such cases with every ventricular systole.

Hypertrophy of Right Ventricle.—The right ventricle will undoubtedly have more to do in such a case than in health, because before the sigmoid cusps will relax, the pressure of the blood within the right ventricle will have to rise superior to that in the pulmonary

artery. Its muscular fibre will therefore tend to hypertrophy as the accompanying figures show :—

	Ventricles.		Walls (Maximum Thickness).	
	Left.	Right.	Left.	Right.
Aortic and mitral both constricted and both incompetent.	3½ in.	3½ in.	+½ in.	+¼ in.

When this hypertrophied muscular fibre contracts, the blood will press injuriously against the tricuspid valve. This valve, at no time, is perfectly competent in Man, and, when increased strain is thus put upon it, it will become much less so than it is naturally. Hence blood will regurgitate and cause the pulsation and other injurious effects so common in such cases. The amount of evil occasioned would thus be proportionate to the extent of the hypertrophy of the right ventricle, and hence the great diversity noticed in regard to the state of the liver, kidney, and other organs, in various forms of valvular heart affection, may be accounted for. In some instances, there is mere congestion of these organs, in others not even this, while, in yet others, they have suffered extreme atrophy.

An emphysematous lung may cause hypertrophy of the right ventricle, accompanied by the same regurgitant effects in distant organs.

The injury is inflicted during the systole of the right ventricle. It is while the contraction of the walls of this chamber is occurring, not while they are in a state of relaxation, that the destructive backward impulse is conveyed to the large veins, rendering their valves incompetent.

If the ventricle failed to empty itself, and if distension of its cavity were thereby occasioned, the tendency to render the tricuspid incompetent would be increased. We do not know, however, whether the ventricle empties itself or not.

It must, moreover, be remembered, that mere distension of the right ventricle would probably never induce a tricuspid regurgitation, if the pressure within the pulmonary vessels remained normal; because the blood, even from a distended ventricle, would by preference run through the pulmonary artery rather than backwards through the tricuspid. Where the pressure within the pulmonary artery is above that of health, the ventricle must contract more energetically to lift the pulmonary artery lock; and even after this has been accomplished, it will continue to be opposed by this over-pressure during the whole time the valve is open. This, in course of time, it is only reasonable to believe, must react injuriously against the tricuspid and add to its natural incompetence.

Conclusions.—The increased work performed by the left chambers of the heart in this form of disease consists in keeping up

the arterial pressure. Part of the energy so liberated is expended upon the pulmonary circulation. By raising the pressure within the pulmonary vessels, this necessitates an increased effort on the part of the right ventricle in opening the pulmonary artery valve, which frequently results in hypertrophy of its walls. The unusually energetic contraction of the ventricle, further, reacts upon the naturally incompetent tricuspid and renders it more incompetent, thus affecting deleteriously the whole venous circulation.

(2) *AORTIC OF NATURAL SIZE BUT INCOMPETENT; MITRAL CONSTRICTED AND INCOMPETENT.*

562. The conditions here, so far as the effects on the right side of the heart are concerned, are probably more favourable than in the former case. As the aortic is of normal size, the blood will pass more easily through its orifice, and, hence, will not tend to regurgitate so freely through the incompetent mitral. The amount of hypertrophy of the right ventricle ought to be less than in the foregoing, because the blood of the right ventricle will, for the above reason, experience less opposition in being propelled into the pulmonary artery. The following are the actual average measurements :—

	Ventricles.		Walls (maximum thickness).	
	Left.	Right.	Left.	Right.
Aortic of natural size but incompetent; mitral constricted and incompetent.	$3\frac{1}{8}$ in.	$+3\frac{1}{2}$ in.	$\frac{1}{8}$ in.	$+\frac{1}{8}$ in.

It might be argued that the wider aortic orifice will allow more blood to regurgitate during diastole; but it is questionable whether this, seeing that the mitral is constricted, would be so injurious in the long run as the regurgitance of the ventricular blood during systole, where, in addition to the mitral constriction, the aortic is also of narrow calibre.

(3) *AORTIC AND MITRAL BOTH CONSTRICTED; AORTIC COMPETENT, MITRAL INCOMPETENT.*

563. The argument based on the figures under Class 2 gains strength from those accompanying this :—

	Ventricles.		Walls (maximum thickness).	
	Left.	Right.	Left.	Right.
Aortic and mitral both constricted; aortic competent, mitral incompetent.	$3\frac{1}{8}$ in.	$3\frac{1}{4}$ in.	$\frac{1}{8}$ in.	$+\frac{1}{8}$ in.

In this case, one element of regurgitant pressure is removed as compared with Class 2, namely, the aortic incompetency. There is superadded another, however, the aortic constriction. The figures remain very much as before, showing that with an incompetent mitral, aortic constriction has much the same effect upon the thickness of the walls and size of the cavities as aortic regurgitance. Where the two conditions of the aortic are combined, however, as in Class 1, the difference in the effects is demonstrated by the greater thickness of the walls, both of the left and of the right ventricles.

(D) Tricuspid Stenosis.

564. The cases of this lesion that have come under the author's personal notice, as before mentioned, have been so complicated with disease of the orifices on the left side, that it is impossible to form an accurate idea of what the result would be on the walls and cavities of the heart.

CONCLUDING REMARKS ON HYPERTROPHY FROM VALVULAR DISEASE.

It must be remembered that the heart, when deprived of its natural locks, may still have a certain inherent power of driving the blood onwards. Just as the œsophagus seizes the draught of liquid and conducts it to the stomach, even against gravity, so the heart may be supposed to do the same with the blood.

Pettigrew has described the ventricle as twisting the mass of blood within it in a spiral manner. If the heart wall has no further hold upon the blood than a mere contractile sac, it is hard to conceive, where perhaps three of the valves are diseased, how the circulation continues to maintain even the desultory course that we know it does.

It should also be borne in mind, that an impaired valve need not be a totally useless valve. It may subserve its purpose in an incomplete manner.

The chief redeeming point in valvular disease of the heart probably is, that the pulmonary cusps are seldom incompetent. This in a manner separates the venous from the arterial circulations and prevents the pressure on both sides from becoming equalised.

CONNECTED TABULAR STATEMENT OF THE WEIGHTS AND MEASUREMENTS REFERRED TO IN CHAPTERS XL. AND XLI., ALONG WITH THOSE OF THE NORMAL HEART.

	Weight in Oz. Avoird.	Orifices.				Cavities.		Walls (Max. thickness)	
		Aortic.	Mitral.	P. Art.	Tricusp.	L. V.	R. V.	L. V.	R. V.
		in.	in.	in.	in.	in.	in.	in.	in.
1. Normal heart . .	10-13	·9-1	1·2-1·4	1·1-1·2	1·5-1·8	3-3½	2 7/16-3⅜	⅜	⅛
2. Aortic of normal size, but incompetent .	21¾	·99	1·3	1·1	1·8	4	4½	⅜	+1/16
3. Aortic constricted and incompetent . .	18¾	·75	1·3	1·1	1·7	3½	3½	⅜	+⅛
4. Aortic dilated and incompetent . .	22¾	1·2	1·7	1·2	2	3¾	3¾	+¼	+¼
5. Mitral constricted and incompetent . .	16	·97	·86	1·1	1·7	+3¼	+3½	⅜	⅛
6. Pure dilatation of mitral . . .	20½	1	1·68	1·27	1·98	3¾	4	+½	1/16
7. Aortic and mitral both constricted, aortic competent mitral incompetent . .	12¾	·7	1	1·1	1·6	3½	3½	⅛	+⅛
8. Aortic and mitral both constricted and both incompetent .	20½	·8	·77	1·08	1·6	3¼	3½	+½	+¼
9. Aortic of natural size, but incompetent, mitral constricted and incompetent . .	20½	·97	·87	1·1	1·6	3½	+3½	⅛	+⅛

HYPERTROPHY AND DILATATION FROM DISEASE OF THE LUNG.

565. (A) **Chronic Bronchitis with Emphysema.**—The general idea is that this combination of disease occasions great dilatation of the right chambers. Gairdner (No. 148, xxiii. 1853, p. 214) said that it is the commonest cause of right-sided dilatation and hypertrophy. Balfour (No. 289, p. 182) asserts that bronchitis is the most frequent means of inducing tricuspid regurgitation. The accompanying figures, derived from a large number of the author's own measurements, it will be observed, bear out, in great part, Gairdner's statement :—

Weight.	Diams. of Orifices.				Cavities.		Walls (Maximum thickness)	
	Aortic.	Mitral.	Pul. Art.	Tricusp.	L. Vent.	R. Vent.	L. Vent.	R. Vent.
+15½ oz.	1 in.	1·4 in.	1·2 in.	1·6 in.	3⅞ in.	3¾ in.	½ in.	¼ in.

It is possible that the dilatation may expend itself partly upon the thin wall of the auricle.

Conclusions.—It will thus be seen that the chief abnormalities consist in a little dilatation of both ventricles together with thickening of the right ventricle; while the orifices remain unaltered. The weight is somewhat increased.

566. (B) **Pulmonary Phthisis.**—The cases from which the following figures were obtained, were instances of ulcerative cheesy pneumonia without much interstitial thickening.

Pulmonary Phthisis.

Weight.	Diams. of Orifices.				Cavities.		Walls. (Maximum thickness)	
	Aortic.	Mitral.	Pul. Art.	Tricusp.	L. Vent.	R. Vent.	L. Vent.	R. Vent.
+ 9¼ oz.	·9 in.	1·2 in.	1·1 in.	1·6 in.	+ 2¾ in.	+ 3½ in.	⅜ in.	⅛ in.

The weight is below average, a fact to be explained by the general emaciation accompanying the disease. The orifices on the left side are somewhat below the average size, while those on the right side do not differ from the normal. Along with the diminution in the size of the orifices, the capacity of the left ventricle is distinctly decreased, while that of the right is just about the average. The wall of the left ventricle is thinner than in the healthy heart.

Balfour (No. 289, p. 182) believes that phthisical disease of the lung does not cause dilatation of the right heart.

Glendinning made the statement that the heart in pulmonary phthisis acquires increased weight. Peacock (No. 209, iv. p. 6) looks upon this as a misinterpretation of facts. In cases of uncomplicated phthisis he declares that the heart is under weight, and often presents the appearance of atrophy. It is only where there has been long standing *obstruction to the pulmonary circulation*, as when one or both lungs are considerably contracted, or when there have been marked bronchitic symptoms, that the heart is found to be enlarged. He admits, however, that if a phthisical lung be accompanied by great impediment to the transmission of blood from the heart, by valvular or aortic disease, the organ may exceed the natural weight, notwithstanding the general emaciation which may be present.

Gairdner (No. 148, xxiii. 1853, p. 225) held views very similar to those of Peacock. He said that "tubercular disease of the lung produces hypertrophy of the heart only when combined with pulmonary atrophy and induration."

Conclusions.—In ordinary ulcerative pulmonary phthisis, the weight of the heart, thickness of the left ventricular wall, and size of the left ventricular cavity and orifices, are all below the normal, a fact which may be accounted for by the general emaciation, and by the blood possibly being less in quantity than in a robust individual.

567. (C) **Chronic Interstitial Pneumonia or Fibroid Phthisis.**—In this disease, the blood-vessels of the lung are much compressed by the cirrhotic tissue. Many of the channels of the middle-sized branches of the pulmonary artery are also constricted or closed from obliterative thickening of the tunica intima. It might therefore be expected that there would be a tendency to dilatation or hypertrophy of the right ventricle. The following figures show that the size of the cavities is unaltered; that the thickness of the wall of the left ventricle is below the healthy average; while that of the right is slightly increased.

Chronic Interstitial Pneumonia.

Weight.	Diams. of Orifices.				Cavities.		Walls. (Maximum thickness)	
	Aortic.	Mitral.	Pul. Art.	Tricusp.	L. Vent.	R. Vent.	L. Vent.	R. Vent.
11½ oz.	·9 in.	1·2 in.	1·1 in.	1·6 in.	3⅛ in.	3¼ in.	+ ⅜ in.	+ ⅛ in.

The weight is not deficient, and the size of the orifices is normal.

Conclusions.—The state of the heart in this disease is practically very much the same as in ordinary pulmonary phthisis.

568. (D) **Stonemason's Lung or Lithosis.**—Not only is the lung intersected in all directions by a dense cicatricial network, but the circulation is still further interfered with by the accumulation of stone dust within it. The state of the heart is represented by the following figures:—

Weight.	Diams. of Orifices.				Cavities.		Walls. (Maximum thickness)	
	Aortic.	Mitral.	Pul. Art.	Tricusp.	L. Vent.	R. Vent.	L. Vent.	R. Vent.
+ 10½ oz.	1 in.	1·3 in.	1 in.	1·7 in.	3⅛ in.	3¼ in.	+ ⅜ in.	⅛ in.

Conclusions.—It would thus appear that, even in this severely obstructive disease, the average weight, size of orifices, capacity of ventricles, and thickness of the ventricular walls are unaltered. The induration of the lung has no positive effect in increasing their dimensions.

Hypertrophy from Adherent Pericardium.

569. This has long been recognised as a cause of hypertrophy. Its origin probably lies in the organ being restrained in its free motion by the attachments to the membrane.

Gairdner (No. 280, 1851) supposed that the free motion of the heart within the pericardium is required in health, not so much to meet the necessities of the circulation in its tranquil and ordinary condition, as to provide for the contingency of excited action, and to give abundant scope for its smooth and painless movement.

HYPERTROPHY OF THE HEART FROM KIDNEY DISEASE.

570. Bright (No. 63, i. 1836, p. 28) first drew attention to the hypertrophy of the heart accompanying chronic disease of the kidney. The disease of the kidney which is oftenest associated with it is **interstitial nephritis**, but various other affections of this organ, if they become chronic, have a like effect.

Stewart (No. 264, i. 1881, p. 388) makes an exception in the case of the **waxy kidney**, which, he says, never leads to cardiac hypertrophy, although he admits that the parenchymatous, when it becomes chronic, does.

Rosenstein (No. 264, i. 1881, p. 388) states, that where the interstitial form of nephritis is complicated with waxy disease, the heart is not hypertrophied.

The absence of hypertrophy in waxy disease of the organ is probably to be accounted for by the ill-nourished condition of the whole body.

Cohnheim (No. 31, i. p. 96) traces hypertrophy of the left ventricle not only to cirrhotic disease of the kidney but to hydronephrosis, *i.e.* a mere obstruction to the free outlet from the gland.

Glomerulo-nephritis, if it last for any length of time, has the effect of inducing enormous hypertrophy. The author's measurements in one most characteristic and uncomplicated case of six weeks' duration showed the following:—

Weight.	Diams. of Orifices.				Cavities.		Walls. (Maximum thickness)	
	Aortic.	Mitral.	Pul. Art.	Tricusp.	L. Vent.	R. Vent.	L. Vent.	R. Vent.
39 oz.	·9 in.	1·4 in.	1 in.	1·5 in.	3¼ in.	3¾ in.	1 in.	½ in.

The obstruction to the circulation in this disease is probably greater than in any other form of nephritis.

In **interstitial nephritis** the following may be taken as representing average measurements:—

Weight.	Diams. of Orifices.				Cavities		Walls. (Maximum thickness)	
	Aortic.	Mitral.	Pul. Art.	Tricusp.	L. Vent.	R. Vent.	L. Vent.	R. Vent.
+ 18½ oz.	·9 in.	1·2 in.	1·1 in.	1·7 in.	3⅜ in.	3⅛ in.	+ ¾ in.	+ ⅛ in.

It would accordingly appear, that while the cavities of the ventricles remain of very much their natural size in this disease, the wall of the left ventricle is nearly twice as thick as it ought to be. The thickness of the right ventricle is only slightly over that of health. The orifices remain of very much the same size as in health. The size of the cavity of the right ventricle, contrary to what might be expected, overpasses that of the left, and the weight is also considerably greater than that of the normal heart.

Stewart (No. 310, p. 233) found hypertrophy of the heart in 46 per cent of a series of cases of kidney disease, and believes that, although not so common in the early stages of the cirrhotic kidney, it is present in almost every advanced case.

According to the principles enunciated under aortic disease (Sect. 551), dilatation ought not to be expected. There is no arterial recoil during diastole—the time at which dilatation is mostly effected.

In aortic constriction with incompetency, two agents are at work in causing the hypertrophy. Here there is only one.

Senator (No. 13, lxxiii. 1878, p. 7) states that *simple hypertrophy* is very often met with in this disease; and he quotes cases recorded by Traube, Dickinson, Bartels, v. Buhl, etc. in support of this view.

Galabin (No. 309) gives the following results from the study of thirty-four cases of contracted kidney:—

Simple hypertrophy of left ventricle . . .	17 times.
Hypertrophy and dilatation of same . . .	5 ,,
Ordinary hypertrophy of heart . . .	6 ,,
,, with dilatation . .	6 ,,

Cause.—There seems to be little doubt that the arterial tension in chronic kidney disease is increased throughout the body. The hard pulse and various other phenomena are indicative of this being the case.

The increased work to be done by the ventricle will then consist in opening the aortic valve, and in driving the blood onwards in opposition to the increased tension. The hypertrophy of the left ventricle may be, and usually is, thus accounted for.

Bright (No. 63, i. 1836) clearly indicated that the hypertrophy of the heart in kidney disease was an effect and not a collateral occurrence. He stated as his belief, that the altered blood of kidney disease so affected the circulation, either through the heart directly or through the smaller vessels, that increased cardiac action was necessary.

Johnson (No. 6, 1877, i. p. 443 *et seq.*) traced the cardiac hypertrophy to stricture of the small arteries caused by hypertrophy of their muscular coats. He made out that the small arteries of the whole body are similarly hypertrophied and their channels narrowed.

Traube's view (No. 316, ii. p. 290), on the contrary, was that the left ventricle hypertrophied, primarily, because the vessels of the kidney were compressed and destroyed; and, secondarily, because the excretion of deleterious substances through the kidney was thus hindered, and consequently altered the composition of the blood.

Then followed Gull and Sutton's observations (No. 34, lv. 1872), by which they

thought to have established that there was a sclerosis of the coats of the small arteries and capillaries ("arterio-capillary sclerosis") throughout the body—an infiltration of a hyaline fibroid substance—which occasioned a universal thickening of the systemic vessels and obstruction to the circulation of the blood. Ewald (No. 13, lxxi. 1877, p. 460) and many others have thrown doubt on this alleged disease of the vessels described by Gull and Sutton; and it is usually believed, at the present day, that the morbid appearances detailed by them are in great part, if not entirely, the result of the reagents in which the vessels were examined.

Ewald (*loc. cit.*) explains the hypertrophy by an alteration of the blood caused through the kidney lesion, whereby it circulates less easily than usual. The arterial system is put upon the stretch, and this has to be compensated for by the increased activity of the heart.

Cohnheim (No. 31, i. p. 97) regarded increased tension of the whole arterial system, on account of the obstruction to the flow of blood through the kidney, as the cause.

Grawitz and Israel (No. 13, lxxvii. 1879, p. 339), as a result of their experiments on animals, found that removal of one kidney, be it from contraction, fatty degeneration, or extirpation, is not followed by cardiac hypertrophy, provided the opposite organ compensatorily enlarges. It may be doubted, however, whether the diseases set up artificially in animals by them were in all respects comparable to those of Man. They state that the arterial pressure did not rise, even after a long period, with a high degree of renal contraction, with chronic parenchymatous nephritis, nor after the extirpation of the organ.

So-called "Idiopathic" Hypertrophy.

571. This term is sometimes applied to the heart when hypertrophied without there being any further disease of its own structure, or of that of other organs.

Increased muscular effort is said to cause it, as when a person, at other times accustomed to a sedentary mode of life, takes to climbing mountains, etc.

Bollinger (No. 49, 1886, Bd. ii. Ab. 1, p. 58) has lately recorded forty-two cases of undoubted simple hypertrophy of the heart without valvular disease. Thirty-eight of these occurred in men and four in women. Taking the normal proportion of heart muscle to body weight as 1 to 216, he finds that the average in these cases was as 1 to 132. The hearts were, therefore, one-third heavier than in health. The subjects of the disease were mostly strongly built, with abundance of subcutaneous fat. His observations were made in Munich, and he regards the great consumpt of beer in that city as the chief cause of the disease. He holds that the liquor acts in a three-fold manner, (1) by the toxic effects of the alcohol; (2) by the quantity of liquid taken into the circulation; and (3) by its affording considerable nourishment.

Hypertrophy a Secondary Affection.

572. It was pointed out by Gairdner (No. 148, xxiii. 1853, p. 225), a good many years since, that dilatation and hypertrophy of the

heart are never other than secondary conditions. This must certainly be true. Hypertrophy of the heart is not a disease; it is a compensatory remedy for disease, and, even although the cause which has induced it be not at once evident, it may be taken for granted that the increase of muscular fibre is simply the expression of some hidden malady.

Heart Disease and Pregnancy.

573. The French school of accoucheurs initiated the view that the left ventricle hypertrophies in the pregnant woman towards the end of utero-gestation (see Bibliography). This notion has been combated by several German obstetricians. Macdonald (No. 311), however, upheld it in this country. The author's own measurements of the hearts of pregnant women at full time, show that the left ventricle has a maximum of three-quarters of an inch, and hence, that it is considerably hypertrophied. The right ventricle does not usually participate in the hypertrophy.

The cause is probably to be sought in the increased work which the heart has to perform in driving the blood through the enlarged uterus.

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Time required for Hypertrophy.

574. Stone makes it out, from a calculation based on some typical cases, to be 1 oz. per week in aortic disease, and half that amount, when it follows upon adherent pericardium. It must be evident that, from so many factors having to be considered, no general rule can be laid down for all cases.

In the instance, quoted at p. 647, of enormous hypertrophy from glomerulo-nephritis, the disease had lasted for about six weeks.

Degeneration of the Hypertrophied Fibre.

575. The statement is almost universally concurred in that the hypertrophied heart is very liable to fatty degeneration, and that this is a common cause of its failure to contract (Cohnheim, No. 31, i. p. 47; Balfour, No. 289, p. 78, and many others). This statement is a vast exaggeration.

Fatty Degeneration of the hypertrophied heart muscle, in

severe obstructive disease of the coronary arteries, or a localised fatty degeneration confined to the tip of a musculus papillaris, as a result of endocarditis, is common enough. A general fatty degeneration of one or both ventricles in hypertrophy from any cause, that is to say, a degeneration capable of inducing appreciable or fatal asthenia, is, however, of rare occurrence. The muscle of hypertrophy is usually typically healthy; it is rigid and well-coloured, and resembles the heart muscle of an ox slaughtered in high condition. The fatty heart, on the contrary, is flabby and anæmic.

Turner (No. 264, i. p. 434) believes that when the hypertrophied heart fails in its action, it is through a general fibroid degeneration of its walls.

Literature on Hypertrophied Heart.—**Auerbach**: Archiv. f. path. Anat., liii. 1871, p. 234. **Bamberger**: Sammlung klin. Vorträge, 173. **Barr**: Med. Times and Gaz., 1876, ii. p. 414. **Biach**: Wien. med. Wochnschr., xxxiii. 1883, pp. 1429, 1461, 1493. **Bollinger**: Deut. med. Wochnschr., x. 1884, p. 180; *also*, Arbeiten a. d. path. Inst. zu München, 1886, p. 501. **Cohnheim**: Vorlesungen üb. allg. Path., i. 1877, pp. 40, 49, 56, 63, 70, 96, 362; ii. 303, 342, 397, 464. **Delafield**: Med. Rec. N. Y., viii. 1873, p. 17; *also*, Am. J. Med. Sc. n. s., xci. 1886, p. 96. **Discussion** (in Relation to Renal Disease): Trans. intern. med. congress, London, i. 1881, p. 364 *et seq.* **Eichorst**: Die trophischen Beziehungen d. Nervi vagi zum Herzmuskel, 1879. **Ewald**: Arch. f. path. Anat., lxxi. 1877, p. 453. **Fraentzel**: Charite-Ann., ii. 1877, p. 339; *Ibid.*, v. 1880, p. 304; vii. 1882, p. 389. **Friedländer**: Arch. f. Physiol., 1881, p. 168. **Galabin**: On the Connection of Bright's Disease with Changes in the Vascular System, 1873. **Goldenberg**: Arch. f. path. Anat., ciii. 1886, p. 88. **Goodhart**: Trans. Path. Soc., xxx. 1879, p. 279. **Bright**: Guy's Hosp. Rep., i. 1836. **Grawitz and Israel**: Arch. f. path. Anat., lxxvii. 1879, p. 315. **Gull and Sutton**: Med. Chir. Trans., lv. 1872. **Israel** (Kidney): Arch. f. path. Anat., lxxxvi. 1881, p. 299. **James**: Med. Times and Gaz., xvi. 1858, p. 586. **Johnson**: Med. Chir. Trans., xxxiii. 1850; *Ibid.*, li. 1868; *also*, Lectures on Bright's Disease, 1873. **Lee (T. J.)**: Richmond and Louisville Med. Journ., xxii. 1876, p. 50. **Letulle**: Recherches sur les hypertrophies cardiaques secondaires, 1879. **Loomis**: Med. Rec. N. Y., viii. 1873, p. 91; *Ibid.*, x. 1875, p. 3; Boston M. and S. Journ., ci. 1879, p. 177. **Pitres**: Des hypertrophies et des dilatations cardiaques independantes des lésions valvulaires. **Rotch**: Cycl. Pract. Med. v. Ziemssen. (Suppl.), 1881, p. 349. **Roy**: Proc. Camb. Phil. Soc., iv. 1881. **Sassezky**: St. Petersb. med. Wochnschr., v. 1880, p. 271. **Senator**: Arch. f. path. Anat., lxxiii. 1878, p. 1. **Smith** (Etiology): Am. Pract. and News, Louisville, ii. 1886, p. 385. **Spatz**: Ueb. d. Einfluss v. Krankheiten a. d. Grösse d. Herzens. Deut. Arch. f. klin. Med., xxx. 1881-82, p. 138. **Stone**: Lancet, 1879, ii. p. 864. **Strauss** (Kidney Lesions in Relation to H., Experimental): Arch. gen. d. méd., 1882, i. p. 5. **Traube**: Ueber den Zusammenbang von Herz-und Nierenkrankheiten, 1856. **Zielonko**: Arch. f. path. Anat., lxii. 1874, p. 29; *also*, Pathologischanatomische u. exper. Studien üb. Hypertrophie d. Herzens, 1875.

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CHAPTER XLII

THE HEART—*(Continued)*

Pathology of Cardiac and Vascular Murmurs.

576. **Definition.**—*In some morbid states of the pericardium and of the endocardium, in connection with lesions of the valves and of the muscular fibre of the heart, and in certain general conditions of debility accompanied by anæmia, the natural sounds heard over the heart and vessels become altered in character, or new and foreign sounds supplant or are superadded to those normally present. Such abnormal sounds are known as murmurs or "bruits." In the case of the heart, the natural sounds may be so slightly modified that the term "impurity of sound" is sometimes applied to the condition.*

Exocardial Murmurs.

577. The heart moves so smoothly within its membranes in health, that no appreciable sound results therefrom. When the pericardium becomes inflamed and fibrinous lymph is precipitated, the roughened surfaces rubbing together give rise to what is known as a **friction murmur.**

The murmur varies in character, being sometimes double or of a to and fro character, that is to say, elicited with the systole and diastole of the heart; at others, there is merely a single murmur synchronous with the systole of the heart. It may be of a harsh, rubbing, creaking, or of a soft and moist nature; or an actual splashing sound may be heard in rare cases, where gas or air is simultaneously present.

If gas or air be mixed with the liquid, over and above the splashing or gurgling sound caused by the motion of the heart, the percussion has been noticed to be tympanitic.

It was originally pointed out by Gibson (No. 58, xii. p. 540) that the murmur of a pericarditis could be distinguished from that due to an endocarditis by its becoming intensified when pressure is made by the stethoscope over the affected area. This

phenomenon may be due to the tissues condensed by the stethoscope conducting the sound from the comparatively superficial pericardium better than from the deeper endocardium.

When pericardial effusion begins to accumulate, it tends to push the lungs aside, and so to increase the extent of cardiac percussion dulness. A considerable quantity, however, may have collected in the sac, without any increase in the percussion dulness being manifest. This is owing to the liquid gravitating to its posterior and inferior parts. Hence it is only when the quantity is excessive that the precordial dulness will be affected.

Endocardial and Vascular Murmurs.

578. **Characters.**—Various fanciful names were formerly applied to endocardial and to vascular murmurs by Laennec, Bouillaud, and others, according to their supposed resemblance to certain familiar sounds. Among these may be particularised the *bruit de soufflet* or *souffle* (bellows-like murmur), the *bruit de scie* (saw-like), the *bruit de rouet* (purring), *bruit de rape* (rasping), the *bruit de diable* (resembling the sound made by a humming top), etc.

These designations, however, apply simply to the quality of the murmur, not to its locality or cause. It is the custom, accordingly, at the present day, to describe murmurs either in terms of their site of maximum intensity and the particular interval of the heart's rhythm in which they supervene, or, it may be, according to their site and probable cause.

Those murmurs which are due to an appreciable morbid lesion are called **organic,** while those, in which such a substratum is wanting, or which are due to some evanescent cause, are known as **functional.**

Organic Murmurs.

579. In connection with the aortic orifice, there may be a **systolic** or a **diastolic** murmur, or the two may be combined; while, corresponding to the mitral, at least three murmurs are generally admitted—a **systolic,** a **pre-systolic,** and a **diastolic.**

The term **direct** is sometimes applied to a murmur, when it is owing to some interference with the flow of the blood in its natural course, while that of **indirect** is sometimes given to a murmur caused by regurgitance.

Flint (No. 314, clxxx. 1886, p. 27) recognises four mitral murmurs, a regurgitant, a direct or pre-systolic, a systolic murmur without incompetence, and a murmur which is diastolic in its occurrence, but not pre-systolic.

"A systolic murmur," he says, "having its maximum of intensity at or near the apex of the heart, transmitted in a horizontal direction to the left of this point, and heard near the lower angle of the scapula, associated with more or less enlargement

of the heart, together with weakening of the aortic and accentuation of the pulmonic sound, is an unmistakable sign of mitral incompetence."

He explains the systolic mitral murmur without incompetence on the ground of intra-ventricular causes, *e.g.* deposit of fibrin on the mitral curtains, the presence of morbid blood, the occurrence of newly-formed bands, etc. in the ventricle. The mitral pre-systolic he traces to vibration of the mitral curtains caused by the mitral direct current of blood being forced by the auricular contraction through a narrow aperture. He accepts as a clinical fact, that mitral stenosis is not always accompanied by a pre-systolic murmur, the conditions for vibration of the valve often not being present. A certain amount of force of blood-current is required in order to excite the necessary sonorous vibration, over and above the mere injury to the valve. He believes the prevalent opinion, that a constriction of the auriculo-ventricular opening is always present in pre-systolic murmur, to be erroneous.

That a *pre-systolic murmur*, when present, is generally the effect of a mitral constriction appears to hold good. In eight cases examined by Gairdner (No. 315, p. 599), and in thirteen by Hayden (No. 288, p. 203), in which a pre-systolic murmur was diagnosed during life, the mitral was found to be constricted.

The pre-systolic *bruit* is most likely due to the narrow mitral allowing a spurt of blood to be injected into the ventricle, and thus exciting a sonorous liquid vein (see p. 656).

Flint (*loc. cit.*) further assumes the murmur which follows the second sound and ends before the contraction of the auricle, if aortic and pulmonary regurgitation be excluded, to be a *mitral diastolic*. It must be caused, he says, "by the current of blood passing from the auricle into the ventricle prior to the auricular contraction." Gravity and the aspiration of the ventricle, he considers, may cause such a current.

Hayden (No. 288, p. 201) supports Flint's view, that a pure diastolic murmur may occur during the passive entrance of blood from the auricle into the ventricle.

FUNCTIONAL MURMURS.

580. These are usually the outcome of some debilitating malady accompanied by anæmia.

Anæmic murmurs are of two kinds—the one heard at the base of the heart, in the second left intercostal space, and from half an inch to an inch and a half beyond the border of the sternum; the other audible over the large veins at the root of the neck, and known from its humming-top-like character as the *bruit de diable*.

A venous murmur, according to Hayden (No. 288, p. 264), "although most frequently heard in the jugulars, is by no means always confined to these vessels; it occurs in aneurismal varix and in the placental and uterine veins in the latter months of pregnancy." He has also heard it in tumours of various kinds.

The site of the basic murmur is described by Latham (No. 318, i. p. 40) as being limited by a line drawn from the left side of the sternum along the upper edge of the second costal cartilage and continued an inch along the second rib; and by another from the sternum along the lower edge of the third costal cartilage continued one inch along the third rib. The inclosed space represents the area where it will usually be heard, and heard most distinctly.

Naunyn (No. 43, v. 1868, p. 189) threw out the suggestion that the murmur was in reality located in the left auricular appendage. In mitral regurgitation not only is the left auricle distended, but also the auricular appendage. When this is so, the auricular appendage twines itself round the pulmonary artery and comes to the surface. Needles pushed through the chest wall at the point of maximum intensity of the murmur, transfixed the left auricle.

It will be found, however, that after death the left auricle in ordinary subjects lies at a good distance from the surface, and would require to be considerably distended in order to approach it. It may be, however, that this distance appears greater after death than it is during life, as the organs tend to collapse and to become retracted when the sternum is removed.

Functional or hæmic murmurs, according to Balfour (No. 289, p. 157), are not always confined to the base, nor are they found to be of maximum intensity over either the aortic or pulmonary area. The *bruit de diable*, or "humming-top murmur," met with in anæmic individuals, is heard not infrequently in the aortic area, more frequently in the pulmonary area, and more rarely in the mitral area.

He draws attention, however (p. 160), to the fact, that the position of maximum intensity of such so-called arterial murmurs is not over any artery at all, but in the second intercostal space, one inch and a half or rather more to the left of the pulmonary area.

He explains this on the theory that the murmur is in reality due to mitral insufficiency, which allows the blood during ventricular systole to regurgitate into the auricle, and that it is rendered evident in the above situation by the distended left auricular appendage coming so close to the surface (as shown by Naunyn, *loc. cit.*). He regards the murmur in this locality as being sometimes the only physical sign of mitral disease. The incompetency of the valve in such cases is brought about by the malnutrition of the muscular fibre either of the heart wall or of the musculi papillares, or by dilatation of the ventricle.

Macalister (No. 6, 1882, ii. p. 821) says it is the base muscles which are at fault. They do not contract sufficiently to approximate the sides of the valve, and hence may render an orifice of natural size incompetent.

Broadbent (No. 6, 1887, i. p. 711), in accepting Balfour's explanation, traces the cause of the deficiency to high arterial tension. Owing to this, the ventricle is unable to empty itself, and hence dilatation follows. High arterial tension, although not invariably an accompaniment of anæmia, is at least of common occurrence.

Balfour's views have been strenuously opposed in various quarters, more especially by Russell (No. 319, i. 1882, p. 97), who has adduced certain objections of considerable weight to Balfour's theory. While not disputing that the murmur heard in a large proportion of cases of debility due to causes such as chlorosis, fevers, and parturition, is excited by a mitral regurgitance owing to laxity of the ventricular walls, yet he denies that its mechanism, as expounded by Balfour, is correct. It is not generally heard at the apex, the point where mitral murmurs are usually loudest, and it has not the purely soft blowing character of a murmur arising in this neighbourhood. It also gradually disappears during inspiration. He explains its

mechanism rather on the assumption that the left auricle becoming distended from the mitral regurgitation, presses injuriously on the pulmonary artery and throws its blood into a state of sonorous vibration.

Gibson (No. 319, i. 1882, p. 86; No. 59, 1877, ii. p. 418) has demonstrated that the cardiographic tracing of the pulsation in the second intercostal space accompanying those cases is decidedly auricular in its character, a fact which would go to support Balfour's theory.

Chauveau supposes that the entire amount of blood in anæmia, in the human subject, is deficient (a statement which would require confirmation), and that this acts injuriously in causing a partial collapse of the capillaries, medium sized arteries and veins, and of the heart with its orifices. The aorta and pulmonary artery are, however, unable to accommodate themselves to the altered conditions as these other parts are, and, hence, as the blood is poured into them from their narrow orifices, it excites a **liquid vein** with its accompanying murmur or *bruit de souffle*.

He would account for the *bruit de diable* on the supposition that the openings of the large veins of the neck do not collapse in the same manner as the rest of the venous system in anæmia, owing to their being continuously united to the deep cervical fascia. The blood returning by them thus discharges itself into an ampulla-like dilatation and a liquid vein is excited.

Dynamic murmurs are such as occur in healthy hearts, probably on account of irregular contraction of the muscular fibres, possibly of the musculi papillares. The murmur which is heard over the heart in chorea has been held by some to be of this nature. Others, however, maintain that it is due to endocarditis.

Physical Causes of Murmurs.

581. **Friction Theory.**—An old notion (Walshe, Gendrin, etc.), which is now pretty well abandoned, was that *friction of the blood against a rough wall* is the cause of intracardiac murmurs. Chauveau's experiments, at least those on arteries, show that this is improbable. He roughened the coat of the carotid in the horse by injuring it, without inducing any murmur; and he placed a piece of metallic tubing, roughened in the anterior, in the course of the artery, with a like negative result.

Corrigan's Theory.—One of the earliest descriptions of what is probably the true explanation of cardiac and vascular murmurs was given by Corrigan (No. 59, April 1829, pp. 1, 33). He demonstrated, that if the subclavian artery be compressed, a loud *bruit de soufflet* is heard, and he explained its occurrence *by the particles of fluid being set in motion with different degrees of rapidity*, thereby causing a sound.

He further demonstrated that when liquid is driven through a membranous tube, such as a piece of intestine, a sound is not elicited so long as the membrane is equally distended, but whenever it is constricted, so as to produce an alteration in the motion of the liquid, a very loud *bruit de soufflet* becomes evident.

Liquid Vein Theory.—When liquid escapes from a narrow

circular aperture in the bottom of a vessel, the stream assumes the following characters: The upper part is smooth and uninterrupted like a glass rod, while the part below is separated into elongated swellings composed, in their turn, of separate drops. The drops are spheroids, and in the middle of the swellings on the jet of liquid, these spheroids are placed with their long axis transversely, being larger here than at either end of the swellings. Between each two drops is one of very minute size.

This phenomenon was first described by Savart (No. 312, 2d series, liii. 1833, p. 337), and the name "veine liquide sonore" was applied to it by him.

Such liquid veins excite *sonorous vibrations*, and consequently, their presence within the heart or vessels has been drawn upon to found a theory of murmurs.

A sonorous liquid vein is caused, not only when a liquid passes through a narrow orifice, but also when such an orifice opens from a narrow vessel into one of wider dimensions filled with liquid.

Chauveau (No. 40, xlvi. May 3, 1858, p. 539), from experiments chiefly made on the horse, came to the conclusion that the *bruits de souffle* are purely physical phenomena, that is to say, that they are sounds subject to ordinary acoustic laws, and that they are engendered by some mechanical cause. This cause does not depend directly upon the quality or quantity of the blood in the vessels, nor upon the state of tension of their walls. Nor does it reside in a roughening of the walls of the vessels, so long as the asperities do not materially modify the calibre of the latter.

When a dilatation exists on the course of a vessel, the blood, on entering this dilated part, can produce a *bruit de souffle*. A narrowing of a vessel more or less extensive may also be accompanied by a *bruit de souffle*, but it is not as the blood enters the narrow part of the vessel, nor in its passage through it, that the murmur is generated, but at that part of the course of the vessel immediately beyond the constriction—a part which, as compared with the constricted portion, presents the conditions of a dilatation. The dilatation may not, therefore, be absolute but only relative. All that is necessary, in order to induce a *bruit de souffle*, is that the difference between the constricted and narrow parts be sufficiently marked, and that the blood penetrate into this dilatation with sufficient force. The greater the force with which the blood is injected, the louder the *bruit*. The injected blood excites a liquid vein with sonorous vibrations.

Talma (No. 169, xxiii. 1880, p. 277) concluded, from his physical experiments, that the *second sound* of the heart is dependent on the vibrations of the liquid, not on those of the valve itself; and that the *first sound* is at least partly due to this. He supposed that heart murmurs are caused in the same manner.

As supporting the view that the pliable texture of the valve is not necessary to elicit the natural or abnormal sounds of the heart, Heynsius (No. 317, 1854, p. 54) held that murmurs could be generated in rigid glass tubes as well as in the more flexible tubes employed by former experimenters. Thamm (No. 43, vi. 1869, p. 129) was of a like opinion, but Weber (No. 138, xiv. 1855, p. 41) looked upon murmurs as the result of vibration of flexible tubes such as the natural vessels represent.

Direction of Murmur.—The murmur is usually propagated in the direction of the flow of blood. When liquid is allowed to circulate

through a tube of narrow calibre opening into a wider tube, the *bruit* excited by the liquid vein is always best heard immediately beyond the narrow tube, in the direction in which the liquid is flowing. When, on the contrary, liquid is made to pass from a wide into a narrow channel, no such vibrations are excited.

Bergeon (No. 313) particularly emphasises the fact that the murmur of a liquid vein is heard only on the distal side of the constriction.

Anæmic Murmurs.—It will be noticed (Sect. 580) that both in Balfour's and in Russell's theories the sonorous liquid vein is assumed to be the actual cause of the anæmic murmur. This notion, however, is not universally accepted.

Thus Hayden (No. 288, p. 248) supposes that there are two factors entering into the causation of hæmic murmurs; first, friction of the blood corpuscles, (*a*) against one another, and (*b*) against the edges of the opening and the walls of the vessel; and, second, vibration of the heart and walls of the vessels. He regards (p. 264) the *bruit de diable* as a sign of absolute reduction of volume or of attenuation of the blood.

It is indeed possible that such attenuation of the blood, by altering its specific gravity, might cause a greater rubbing of the corpuscles against the vessel walls than usually happens. Whether, in doing so, they would excite a murmur may well be questioned. There cannot be much, if any, doubt that the altered condition of the blood has in some way to do with the generation of the abnormal sound, for if an animal be bled until it is feeble, an anæmic murmur becomes apparent; while, if large quantities of water or salt solution be injected into its vessels, so as to compensate for the loss, the murmur does not disappear. It does not disappear in fact until the blood has recuperated itself through the lapse of time (Richardson, No. 185, 1868; Macalister, No. 6, 1882, ii. p. 825).

Musical Murmur.—Where the murmur has a musical character, it will generally be found that a portion of valve or endocardium has been hanging loose in the blood current, and has been in a state of rapid vibration, or that a valve has been perforated. The former is perhaps the commoner of the two causes.

Schroetter (No. 49, 1883, ii. p. 150) distinguishes musical systolic and musical diastolic murmurs. In the former, he usually found a tendinous band stretching across the ventricle; in the latter, a thread-like filament coming off from the posterior cusp of the aortic valve, which by its vibrations had evidently given rise to the sound.

v. Drozda (No. 49, 1883, ii. p. 142) describes mitral systolic murmurs as being caused by (1) a cicatricial band stretching across the left ventricle, which becomes alternately stretched and relaxed with the movements of the heart; (2) stretching of hypertrophied and retracted chordæ; (3) undue pressure in an otherwise healthy ventricle. He finds musical diastolic mitral murmurs in various degrees of constriction of the orifice. He accounts for aortic musical murmurs by (1) tendinous or band-like connections of the aortic cusps to the aorta or to each other; (2) calci-

fication of ascending aorta ; (3) stenosis of ventricular ostium ; (4) congenital bands stretching between the ventricle and aorta.

Musical diastolic aortic murmurs he finds (1) in partial destruction of the free border of the valve ; (2) in fenestrated valves.

Pucci (No. 49, 1885, ii. p. 166) found a perforation of an aortic cusp in a case where the murmur resembled the cooing of a dove.

Prolongation of the First Sound.—This is frequently heard a few days after an acute endocarditis has commenced. Sansom (No. 295, p. 21) accounts for it by an impairment of the natural valvular element of the sound. The curtains of the valve being swollen, the sound elicited by their closure is not so sharp as in health.

Harsh and Grating Murmurs.—Hayden (No. 288, p. 184) explains these by "the attrition of two uneven and dense surfaces against one another, or of a strong current upon solid, rugged, or projecting points of surface. Soft murmurs, on the other hand, are caused by the movement of currents over smooth and even surfaces."

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CHAPTER XLIII

THE BLOOD VESSELS

THEIR NORMAL STRUCTURE

582. **Arteries.**—When a cross section of a branch of a middle-sized cerebral artery, taken from the base, is examined microscopically, it is seen to be composed essentially of four coats: (1) the **tunica intima** with its endothelium; (2) the wavy **inner elastic lamina**; (3) the **muscularis**; and (4) the areolar sheath or **tunica adventitia**. In some arteries, such as the renal, there are several elastic laminæ. In the largest arteries, the muscularis is poorly developed. Although the coats of the artery have sometimes been more minutely subdivided, it will be found that the above is sufficient for pathological purposes.

Veins.—These differ from the arteries chiefly in the greater thinness of their walls. The muscularis is less developed, but the adventitia is relatively thick.

Capillaries.—The capillaries consist of a single layer of elongated endothelial cells. In some localities, the larger capillaries have a thin adventitia around them.

THEIR NERVE SUPPLY.

The nerves controlling the **arteries** are of two kinds, namely, vaso-constrictors and vaso-dilators.

The vaso-constrictors are connected in the following manner with the cerebro-spinal nerve centres. The great vaso-motor centre is located in the medulla oblongata, while several minor centres are evidently placed in the gray matter of the spinal cord. The former is most likely in communication with the higher encephalic centres. Some of the fibres emanating from it are distributed, along with the cranial nerves, to the organs which the latter supply (eye-ball, tongue, etc.), while others run down in the lateral column of the spinal cord,

join with its vaso-motor nuclei, and either pass into the peripheral nerves by the anterior spinal roots or join the sympathetic through the rami communicantes. They ultimately terminate in the muscular coat of the arteries.

The vaso-dilators are most likely connected with a centre in the medulla oblongata, although this has not been proved. They issue along with certain of the cerebral and spinal nerves. Their function is to bring about a relaxation or inhibition of the muscular fibre of the arteries, and, hence, they are antagonistic to the vaso-constrictors. They are evidently more abundant in certain localities than in others.

The veins also contain nerve fibres, but they are fewer in number.

The capillaries, so far as is known, are unprovided with any nerve supply.

ARTERIES—INFLAMMATORY AFFECTIONS—ARTERIITIS

(*ἀρτηρία, an artery*).

583. Several varieties of inflammation of the arteries are usually described, such as: (1) the atheromatous; (2) the obliterative; (3) the acute suppurative; (4) the warty; and (5) the malignant; (6) a periarteriitis; or (7) a periarteriitis nodosa.

(1) *ATHEROMATOUS ARTERIITIS.*

(*Endarteriitis chronica nodosa s. deformans.—Virchow*)

Naked-Eye Appearances.—The disease is primarily one of the inner coat. As this, like the endocardium, is devoid of blood-vessels, it follows that congestion cannot be the first indication of its being inflamed.

The earliest sign of the disease is a **milky opacity of the tunica intima,** an appearance similar to that noticed in the commencement of endocarditis. The milky opacity is never universal over a large area, but is confined to patches here and there. These patches soon become converted into elevations from the thickening which takes place in the membrane.

A **pale yellow spot** next appears in the centre of each patch, and this spreads throughout all its substance. The change in colour indicates that the thickened patch has become fatty or **atheromatous** as it is called (*ἀθήρη*, gruel or pap).

The vessel now presents a somewhat deformed appearance. If it be a cerebral artery, these yellow thickenings destroy its even contour, and are visible from the outside. They seldom, however, extend round its entire circumference. The intima of the whole aorta may be covered with them.

They are sometimes in the form of button-like elevations, located

around the openings of the branches of the artery. The intercostals are occasionally surrounded by these at their points of origin.

The fatty patch of thickening may either **ulcerate** or **calcify**. Where ulceration occurs, it shows itself first at the centre. The fatty part softens and discharges its contents into the channel of the vessel. A ragged ulcer, with undermined edges and a rough floor, is thus left, whose margins may subsequently become calcareous; or the ulcer may penetrate deeper, and by thus weakening the wall, predispose to **aneurismal dilatation.**

The patch may also calcify without ulcerating, thus constituting

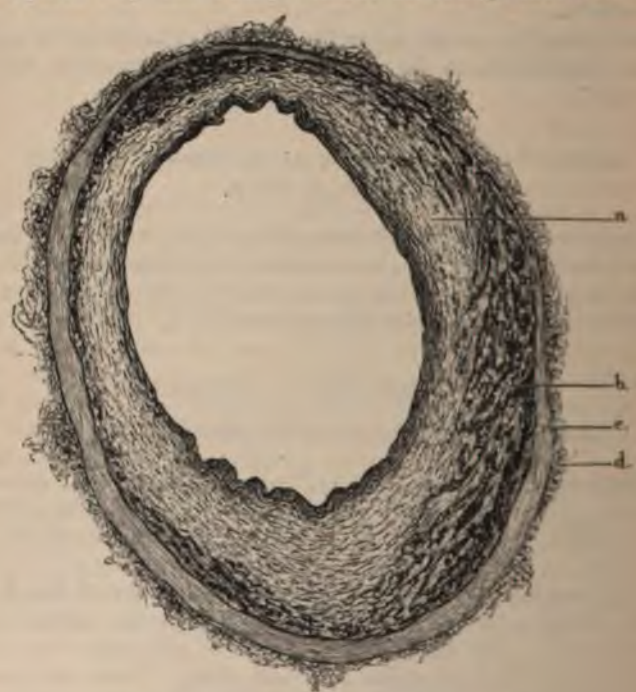

FIG. 196.—ATHEROMATOUS ARTERITIS (×40 DIAMS.).]

(*a*) Unilaterally thickened tunica intima; (*b*) atheromatous part of same; (*c*) muscularis attenuated opposite the atheromatous part; (*d*) tunica adventitia comparatively unaltered (unstained).

a **calcareous scale.** Such scales are liable to become dissevered from their attachments, and may then be carried off as emboli with the blood stream.

Microscopic Appearances.—The thickening presents a cicatricial structure. Numbers of round and spindle-shaped cells with delicate bundles of fibrous tissue chiefly compose its substance. There is an absence of blood-vessels within the thickening, a circumstance which may account for its inherent tendency to become fatty.

The atheromatous degeneration always commences at the part of the thickened intima farthest away from the blood stream, that is to say, at the part nearest the muscularis. It usually destroys the inner elastic lamina as well as the sclerosed intima. A few black spots make their appearance, which shortly afterwards coalesce. The tissue disintegrates and softens, and a small cavity results. Within this cavity are contained granular débris, oil globules, and, pretty often, cholesterine crystals. The free surface of the thickened intima often remains unbroken until the fatty degeneration has proceeded far within the deeper parts. The muscularis may subsequently become involved in the degeneration.

Sites.—The *arch of the aorta* is undoubtedly the commonest, and the descending portion of the same vessel comes next. The *iliacs* are frequently affected, and the *cerebral arteries* at the base are specially prone to the disease. The *arteries of the limbs* do not suffer so frequently, nor does the *pulmonary artery*, although, if the latter be carefully examined, it will be found to be more commonly atheromatous than is ordinarily supposed (see Rattone, No. 133, ix. 2, 1885).

Effects.—Loss of elasticity might of course be presumed to be, and actually is, a common result. Where the disease is at all advanced, more or less distension of the affected vessel will usually be found, and this frequently assumes the form of an aneurism. The disease is, in fact, the usual predisposing cause of aneurism.

Causes.—Both this and the obliterative form of arteriitis are said to be *syphilitic* in their origin. The atheromatous variety, however, is certainly not always so. It seems to be, most often, a disease of old age. It is more common in males than in females. Gout and rheumatism have been alleged to predispose to it. Israel's experiments (No. 13, lxxxvi. 1881, p. 299) seem to show that it is also connected with chronic disease of the kidney.

Simple Fatty Degeneration of Intima.

In a large number of aortæ small superficial streaks or minute patches, with, occasionally, a trellis-work-like or feather-like arrangement, will be detected. They occur in individuals past middle life with great frequency, and Virchow (No. 236, p. 15) has drawn attention to their presence in young chlorotic persons. They cannot be regarded in the same light as the raised fatty patches just described in endoarteriitis. They appear rather to be points of simple fatty degeneration of the intima.

Literature on Atheromatous Arteriitis.—**Coats**: Glasg. Med. Journ., xxvii. 1887, p. 265. **Cohn** (Bone Formation in): Arch. f. path. Anat., cvi. 1886, p. 378; *also*, Ueb. d. Verchnöcherung d. Arterien, 1886. **Greenfield**: Trans. Path. Soc. Lond., xxvi. 1875, p. 135. **Gutmann**: Ueb. chron. Endoarteriitis, 1874. **Israel**: Arch. f. path. Anat., lxxxvi. 1881, p. 299. **Lister** (Coagulation in): Edin. Med. Journ., iii. 1858, p. 893. **Löwenfeld**: Wien. med. Wochenschr., xxvii. 1877, pp. 991, 1015, 1039. **Martineau** (Pulm. Artery): Compt. rend. Soc. de Biol., iii. 1862, p. 163. **Mayet** (Pulm. Artery):

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(2) *ARTERIITIS OBLITERANS.*

584. **History.**—In the year 1874, Heubner (No. 327) published an elaborate monograph on the subject of the obliterative inflammation from which the arteries of the brain suffer in tertiary syphilis. Wilks (No. 63, ix. 1863, p. 45) had previously drawn attention to the disease, which he described as being "of a fibroid character exemplified by a thickening of the coats of the vessels and the proportional diminution of their calibre." He also distinguished between this variety of arteriitis and the atheromatous. Moxon (No. 59, 1869, ii. p. 435) had likewise given a graphic description of the naked-eye appearances of the disease.

To Heubner, however, is due the credit of demonstrating that the disease essentially consists in an obliterative thickening of the tunica intima. That there is a special form of obliterative arteriitis associated with syphilis does not appear to have been clearly recognised previous to Heubner's publication, many as the works have been on the subject.

Since then, the disease has been shown by Friedländer, Greenfield, Gowers, Baumgarten, and many others (see Bibliography) not only to be associated with syphilitic deposits, but to have a much wider range in pathology.

FIG. 197.—NODULAR THICKENINGS ON SYPHILITIC ARTERIES OF THE BRAIN.

Naked-Eye Appearances.—The vessels of the brain must be regarded as those in which the disease develops itself most typically. It affects the small arteries by preference. They present a universal cord-like hardness, their lumina may just be perceptible or may be quite closed, and there is an absence of the yellow patches seen in the atheromatous disease.

Although the outline of the vessel is, as a rule, uniform, yet it may happen, that, here and there along its course, there are annular thickenings. These are the result of a cellular deposit in and around the tunica adventitia.

Baumgarten (No. 13, lxxxvi. 1881, p. 186) refers specially to these, and gives a drawing of them (see Fig. 197). He looks upon them in the light of small gummata.

Microscopic Characters.—The disease, like the atheromatous, is essentially one of the **tunica intima**, but, as just said, the **adventitia** may also become infiltrated with the syphilitic effusion. The

intima assumes the same sclerous appearance as in the atheromatous disease with the exception of the thickening being uniform and not becoming fatty. The thickened intima has a tendency to encroach more and more upon the channel of the vessel, and finally to obliterate it. Small blood-vessels are also projected into it from the other tunics, and it is, probably, on this account that the thickened intima does not become atheromatous.

It seems likely that all the nucleated structures of the intima participate in forming the new tissue. The inner elastic lamina remains completely unaltered. It is questionable whether the endo-

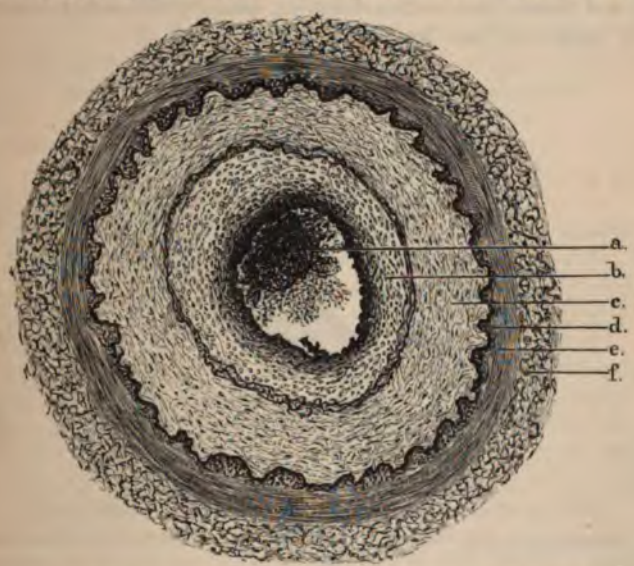

FIG. 198.—ARTERIITIS OBLITERANS, SYPHILIS OF BRAIN (×50 DIAMS.)

(a) blood-clot; (b) inner layer of thickened tunica intima; (c) outer layer of same; (d) inner elastic lamina; (e) muscularis; (f) thickened adventitia (Perosmic acid and Farrants').

thelium actually takes part in the thickening. It probably does not, because the interior of the vessel always has a perfectly smooth outline.

The **muscularis** is seldom affected, but the adventitia is not infrequently pervaded with a small cell effusion, which accumulates at parts, so as to give rise to the nodular swellings before referred to.

Points of distinction between this and the Atheromatous.—(1) The disease affects small arteries in preference to large; (2) the thickening of the intima is symmetrical; (3) the sclerous tissue becomes vascular and does not tend to fatty degeneration; (4) the disease results in obliteration of the channel of the artery, and does not predispose to aneurism; (5) it is usually accompanied by other unequivocal signs of the syphilitic constitution.

Causes.—*Tertiary syphilis* may be said to be the most direct, and that which acts most universally.

In *cirrhosis of the kidney* a thickening of the inner coat, in appearance similar to that of syphilis, is constantly found. In the ulcerating parts of a *phthisical lung* many of the branches of the pulmonary artery are in a state of complete obliteration from a like thickening of their inner coat. The *vessels of the fœtus* which become functionally inert after birth, are closed by the same means; and the arteries of the *pregnant uterus*, become reduced in size and in part closed, subsequently to utero-gestation, by a similar thickening of their intima. *Ligatured vessels*, and those filled with a *thrombus*, heal by the same hyperplasia of their inner coat (see Sects. 210 and 211).

FIG. 199.—CLOSURE OF A SMALL ARTERY AFTER LIGATURE (×40 DIAMS.)

(*a*) Tunica adventitia; (*b*) thickened tunica intima; (*c*) inner elastic lamina (Picro-carmine and Farrants').

It may be questioned, however, whether the thickening of the intima can be regarded as inflammatory or reactive. It often looks more as if it were an overgrowth of fibrous tissue, caused by the blood ceasing to circulate through the vessel.

Effects.—As the arteries in course of time become impervious, it naturally follows that the nutrition of the parts supplied by them must be impaired. In the case of the brain, circumscribed softenings are among the commonest results. They give rise to local paralysis of the various cranial nerves. When the root of the fifth becomes involved, severe cephalic neuralgia may be one of the most prominent symptoms. Where the disease occurs in process of ulcerative destruction of an organ, such as that of a tubercular lung, it may have a salutary effect in preventing fatal hæmorrhage. As a strictly analogous process constitutes the means by which arteries are closed when ligatured, and by which the temporary vessels of fœtal existence are

obliterated, it subserves a useful purpose in these cases. It seems, also, in a manner, to lend additional support to the branches of the renal artery in cirrhosis of the kidney, and thereby aids in preventing dilatation.

Literature on Arteriitis Obliterans.—**Baumgarten:** Arch. f. path. Anat., lxxiii. 1878, p. 90; *Ibid.*, lxxvi. 1879, p. 268; lxxxvi. 1881, p. 179 (see other references in Bibliog. accompanying the last). **Biach** (Pulm. Art. Stenosis): Mitth. d. Ver. d. Aerzte in Nied-oest, Wien, xi. 1885, p. 297. **Bristowe:** Trans. Path. Soc., x. 1859, pp. 21, 44, and 57. **Friedländer:** Centralbl. f. d. med. Wissensch., xiv. 1873, p. 65. **Gowers:** Trans. Path. Soc., xxviii. 1876-7, p. 286. **Greenfield:** Trans. Path. Soc. Lond., xxviii. 1876-7, pp. 258, 272. **Guenau de Mussy:** Arch. gén. de méd., 1872, ii. p. 129. **Heubner:** Die luetische Erkrankung d. Hirnarterien, 1874; v. Ziemssen's Cyclop., Eng. Trans., xii. 1877, p. 293. **Jackson (H.):** Lond. Hosp. Rep., 1868. **Middendorp** (Pulm. Art. Stenosis): Internat. Monatschr. f. Anat. u. Histol., iii. 1886, p. 239. **Moxon:** Lancet, 1869, ii. p. 435. **Peabody:** Med. Rec. N. Y., xxx. 1886, p. 65. **Saundby:** Journ. Anat. and Physiol., xvii. 1882-3, p. 180.

(3) *ACUTE PURULENT ARTERIITIS.*

585. This is usually an accompaniment of pyæmia.

According to Jaccoud (No. 330, p. 813), the disease is ushered in by an injection of the vasa vasorum. The coats of the artery become acutely inflamed. Pus forms between them, and often spreads so as to dissect the one from the other. An abscess may develop round the artery.

The intima becomes roughened from the multiplication of cellular elements upon its surface (Cornil et Ranvier, No. 255, p. 493).

A clot is usually precipitated over the roughened wall of the vessel, partially or completely obliterating the channel. There is sometimes an intimately adherent thrombus with a secondary clot over it. (Consult Virchow, No. 13, i. 1847, p. 272).

Literature on Acute Suppurative Arteriitis.—**Cornil and Ranvier:** Manual Path. Histol. (Eng. Trans., 1882), p. 491. **Jaccoud:** Traité de path. interne, 1877, p. 813. **Stroganow:** Arch. d. physiol. norm. et path., iii. 1876, p. 325. **Virchow:** Arch. f. path. Anat., i. 1847, p. 272.

(4) *ENDARTERIITIS VERRUCOSA.*

586.—Under the term "Endartérite verruqueuse," Lancereaux (No. 329, Pl. xxiv. Fig. 2) figures a condition of the femoral artery characterised by rounded wart-like projections on the intima with patches of what he calls vascular injection here and there. Zahn (No. 13, lxxii. 1878, p. 214) describes a very remarkable instance of the disease, in which, growing from the intima of the aorta and iliacs, there were several of these rounded wart-like projections. They varied in size from a pin's head to a pea, the vessels from which they sprang being otherwise healthy. They had a smooth surface, and were of the same colour as the tunica intima.

He thinks it possible that they may have been organised thrombi,

and doubts whether the nodular masses described by Lancereaux were of the same nature.

(5) *ACUTE MALIGNANT ARTERIITIS.*

587. A disease similar to malignant endocarditis is occasionally, although rarely, met with in the aorta (acute aortitis). As in malignant endocarditis, it may possess a proliferative or an ulcerative tendency. Vegetations of a fleshy consistence are found situated either on an acutely indurated and thickened patch of the intima, or upon an old abrasion caused by previous atheromatous degeneration. They are identical in structure with endocardial vegetations.

Borneque (No. 49, 1883, ii. p. 158) states that in acute aortitis new blood-vessels may permeate the entire wall of the vessel.

Micro-organisms are usually found in abundance on the surface and within the substance of the vegetations. There is always some source of septic contamination.

(6) *PERIARTERIITIS (CHARCOT).*

588. The suppurative form of inflammation of arteries is often mainly localised in the adventitious coat or in the adjacent areolar tissue. Charcot, however (No. 331, p. 284), has described another form of periarteriitis which is not suppurative but which leads to **miliary aneurism**. The vessels of the brain are its special seats. The disease may possess all the coats of the vessel, but does not affect them simultaneously. It progresses from without inwards, and commences by a small-cell deposit in the adventitious coat. At other times, however, there is only a more or less marked thickening of the membrane, so great that it may be equal to the calibre of the vessel. This cellular accumulation in the adventitia tends to cause atrophy and weakening of the muscularis, and, so, predisposes to aneurismal dilatation (see *miliary aneurism*). The inner coat is least seldom affected.

The capillary vessels are sometimes similarly diseased, or, it may be, the larger arteries at the base. The small arteries, however, are those in which it commences and is best marked.

(7) *PERIARTERIITIS NODOSA.*

589. Kussmaul and R. Maier (No. 208, i. p. 484) describe a peculiar disease of the arteries, chiefly of arteries of like or of less calibre than the coronary, and specially of those supplying the intestine, stomach, kidneys, spleen, heart, and voluntary muscles. They give it the above designation.

The vessels are at some points dilated, at others contracted, so as to cause great deformity. The outer coat of the vessel is diffusely

infiltrated with a cellular deposit, the muscularis is fatty, while the intima is comparatively unaltered.

P. Meyer (No. 13, lxxiv. 1878, p. 277) recounts the particulars of what appears to have been an instance of this disease. There were oval or rounded tumours of various size upon several different arteries supplying such parts as the muscles, the thyroid gland, the tongue or mucous membrane of the pharynx, and upon the smaller arteries of the abdomen, etc. The nodules were aneurismal, and, the muscular coat being ruptured, their wall was mainly composed of the adventitia. The adventitia was infiltrated with cells, and the sac frequently contained a thrombus.

Calcification.

590. As a result of atheromatous endarteriitis, the thickened patches on the affected vessel usually become calcareous. It by no means always happens, however, that the impregnation is a result of atheroma. Many arteries seem to become calcareous without any preceding disease. The small arteries and capillaries of the brain are occasionally so calcified that they project as bristle-like bodies when the organ is incised. The radials are also frequently calcareous throughout their entire course; and, in such cases, the infiltration is so universal that, when dried, the vessel may resemble a tube almost continuously calcic.

Not only an impregnation of the coats of the vessel may take place—a mere calcification—but a true **bone-formation** may also ensue. Cohn (No. 13, cvi. 1886, p. 378) describes and figures such bony deposits in arteries, and the condition is also referred to by Orth (No. 328, i. p. 225).

An artery which is merely hypertrophied and under high tension is often mistaken during life for one which has become calcified.

Literature on Calcification and Ossification of Vessels.—**Cohn** (Ossification): Arch. f. path. Anat., cvi. 1886, p. 378. **Förster:** Atlas d. mik. path. Anat., 1854. **Hubrich:** Zeitschr. f. Biol., ii. p. 377. **Küttner:** Arch. f. path. Anat., lv. 1872, p. 521. **Sankey** (in Brain): Trans. path. Soc., xvii. 1866, p. 8. **Simon:** Arch. f. path. Anat., lv. 1872, p. 534. **Virchow:** Arch. f. path. Anat., viii. 1855, p. 103.

Hypertrophy of Muscular Coat.

591. Wherever increased strain is brought to bear upon the wall of an arteriole from the blood within it, there is a tendency to its muscular coat becoming hypertrophied. In *cirrhosis of the kidney*, the small branches of the renal, and many of the arteries throughout the body, become thickened from this cause. In *cirrhosis* and various other diseases of the *lung*, the small branches of the pulmonary also react in the same manner. In *chronic lead poisoning*, there is also a tendency to a general hypertrophy, but it is a question whether this may not be in great measure dependent upon the cirrhosis of the kidney which so often accompanies the disease.

The increase in the fibre appears to be numerical.

Johnson (No. 192, xxviii. 1877, p. 381) supposes that the hypertrophy of the peripheral arteries in cirrhotic disease of the kidney is due to their being thrown into contraction by having to circulate impure blood.

ANEURISM—(*ἀνεύρισμα, a widening*).

592. **Definition.**—The local dilatation of an artery or set of arteries into a tumour-like sac; or the production of a sac from the surrounding tissues which is permeated by circulating blood derived from an adjacent artery.

Varieties.—The terms *true* and *false aneurism* are often employed. By the former is meant an aneurism whose wall is composed of any of the coats of the artery in which it originated; by the latter one in which the wall is the result of a condensation and adhesion of the neighbouring tissues.

A *fusiform aneurism* is one in which the distension of the vessel is uniform. It has an oval or spindle shape.

A *saccular aneurism* is a rounded sac springing from one side of the artery.

The term *cirsoid aneurism* (κιρσός, varix) is applied to a pulsating vascular swelling, due to a number of small arteries in a particular locality having become dilated.

By *varicose aneurism* (aneurisma varicosum) is understood a condition in which an aneurism becomes adherent to a vein, and where, in course of time, a communication is established between them. The aneurism, in such a case, may be true or false.

The term *aneurismal varix*, on the other hand, is applied to the tumour which results from an artery and vein having been simultaneously wounded, as in performing phlebotomy at the bend of the arm. The arterial blood is poured into the vein, which becomes distended into a varix or aneurism-like pouch by the increased pressure from within.

A *dissecting aneurism* is caused by the blood forcing its way between the coats of the artery and separating them. Dissecting aneurisms are common in the brain.

The expression *diffuse aneurism* is sometimes employed to describe a false aneurism which has spread widely along the sheaths of muscles or other natural barriers.

Sites.—The commonest are (1) the arch of the aorta; (2) the vessels of the limbs and neck; and (3) the cerebral arteries.

That of the **aortic arch** may be composed of the coats of the vessel, or the greater extent of the sac may be constituted by the adherent boundaries of one of the mediastina. The opening in the wall of the vessel, in the latter case, has often a punched-out character, the margins of its stretched and lacerated tissues being continuous with the false part of the sac.

The aneurism is seldom situated on the intra-pericardial part of the

vessel, but, more commonly, upon the upper end of the ascending and upon the transverse part of the arch.

It sometimes reaches an enormous size, and may thus press against the sternum. The sac becomes adherent to the bone, and, in course of time, erodes it so completely that it may protrude through it. Rupture of such an aneurism, however, even where it has come close to the surface, is rare. It may leak from time to time, but sudden rupture is unusual.

Aneurisms of the descending part of the aorta are usually adherent to the spinal column. One or more of the bodies of the vertebræ are liable to erosion; the spine, in fact, may constitute the posterior boundary of the sac.

Aneurisms of the limbs or neck are commonly saccular. The parts which are pushed aside by the sac are often condensed into a spurious capsule.

Contents.—More or less old laminated clot will, as a rule, be found within the sac, often with a mass of recent coagulum. The laminæ become much condensed in old aneurisms, and assume a half-fibrous appearance. In a large sac, like that of an aortic aneurism, they do not show the slightest tendency to organise (see p. 302). The wall of the sac is in such a morbid state that it fails to furnish the necessary elements for organisation.

Such dense laminated clots, however, subserve a useful purpose in compensating to a certain extent for the lost resistance of the distended vessel. They may lie in the sac for months, and even, there is good reason to believe, for years, without suffering any degenerative change.

Hyaline degeneration of the contents is described by Meyer (No. 4, vii. 1880, p. 598). The thrombus becomes permeated by a network of canals in which the hyaline substance accumulates.

Cause.—The starting point of most of the aneurisms of the larger trunks is an atheromatous endo-arteriitis. This weakens the coats of the vessel, and allows the arterial blood pressure to force the wall outwards.

Relation to Sex.—Aneurisms of the aorta and other large trunks are commonest in males. It has been asserted that the reasons for this are, that males suffer more often from syphilis than females, and that they are exposed to greater muscular strain from the nature of their avocations.

CEREBRAL ANEURISMS.

The main branches of the cerebrals at the base are occasionally the seat of moderate or even large-sized aneurisms. Coats (No. 264, 1881, i. p. 415) has drawn attention to these as a cause of cerebral hæmorrhage, and Bramwell (No. 19, xxxii. 1886, p. 911) and others, have recorded aneurisms in this locality of great bulk. It is probably because they

receive such equable support on all sides, that the basal vessels, which suffer so commonly from atheromatous disease, are not oftener aneurismal.

A more usual form of aneurism of the cerebral vessels, however, is that figured by Cruveilhier (No. 332, Pt. xxxiii. p. 442), and originally described by Virchow (No. 13, iii. 1851, p. 427), which, in later times, was made a subject of special study by Charcot and Bouchard (No. 333; *also*, No. 4, i. 1868, pp. 110, 127 *et seq.; also*, No. 331, p. 291). The name **miliary** is usually applied to these aneurisms. They are almost always multiple, and are most often seen upon the surface of the convolutions or at the depths of the sulci. They may be situated superficially over the basal ganglia, in their substance, or in that of the hemispheres generally. They are often over a hundred in number, and can be readily detected with the naked eye, being from $\frac{1}{30}$ to $\frac{1}{4}$ mm. in breadth. They are either saccular or fusiform in shape, and are a frequent cause of cerebral hæmorrhage.

Charcot traces their origin to a periarteriitis. The media becomes weakened from the infiltration of the adventitia, and allows the expansion to take place.

Literature on Aneurism of Vessels.—Consult the various Text-books on Surgery, and **Barlow**: Transact. Path. Soc., xxix. 1878, p. 8. **Bartholow**: Am. Journ. Med. Sc., 1872; Rev. Sc. méd., 1873, i. p. 149. **Bouchard**: Recherches sur quelques points de la pathogénie des hémorrhagies cérébrales, 1866; *also*, Eng. Trans., 1872. **Bramwell** (Enormous Intracranial) Edin. Med. Journ., xxxii. 1886, p. 911. **Church**: St. Barth. Hosp. Rep., vi. 1870, p. 99. **Coats** (A. and Cerebral Hæmorrhage): Trans. Internat. M. Cong. Lond., 1881, i. p. 415. **Charcot** (Miliary Brain): Senile and Chronic Disease, New Syd. Soc., 1881. **Charcot and Bouchard**: Arch. d. phys., i. 1868, pp. 110, 127 *et seq.* **Cruveilhier** (Miliary): Anat. path., ii. 1835-42, livr. xxviii. pl. 3, fig. 2. **Eichler**: Deut. Arch. f. klin. Med., xxii. **Eppinger** (Miliary): Arch. f. path. Anat., cxi. 1888, p. 405. **Fagge**: Med. Chir. Trans., 1869. **Friedländer**: Arch. f. path. Anat., lxxviii. 1879, p. 357. **Gee**: St. Barth. Hosp. Rep., vii. 1871, p. 147. **Hunter (W.)**: Med. Observ. and Inquiries, ii. 1762. **Krauspe** (Diffuse Widening): Berl. klin. Wochnschr., x. 1873, p. 121. **Legg and Ormerod**: (Brain Vessels) St. Barth. Hosp. Rep. xii. p. 239. **Liouville**: Anéurysmes miliares. Thèse de Paris, 1871. **Meyer** (Multiple): Arch. f. path. Anat., lxxiv. 1878, p. 277. **Morvan**; De l'anéurysme variqueux, Thèse de Paris, 1847. **Pemberton**: Med. Chir. Trans., xliv. 1861. **Quincke**: v. Ziemssen's Cyclop., vi. 1876, p. 345. **Stimson** (Arterio-venous, Carotid, and Jug. Vein): New York Med. Journ., xxxviii. 1883, p. 611. **Virchow**: Arch. f. path. Anat., iii. 1851, p. 427. **Ziegler**: Text-Book Path. Anat., Eng. Trans., Sect. 1-8, 1884, p. 75.

Arterio-Capillary Fibrosis.

593. In the year 1872, Gull and Sutton (No. 34, lv. 1872, p. 273) described what they called a fibroid degeneration in the arterioles, capillaries, and interstitial tissue of various organs; (1) in notorious cases of contracted kidney; (2) in others where the kidneys were but slightly affected, and yet in which the heart was hypertrophied; and (3) in cases where the heart was hypertrophied without the presence of contracted kidney.

They believed that it was a general disease affecting the small arteries throughout the body, and that the cirrhotic disease of the kidney was not purely and essentially renal, but simply part of a universal arterial fibrosis. The organs in which they found the arteries so affected were the stomach, spleen, liver, lungs, heart, cord, brain, and skin.

The coat of the vessel most implicated is the adventitia, but sometimes the other tunics suffer. The vessel, besides being fibrous, assumes a hyaline appearance—hence the term they employ, "hyaline fibroid."

The author never remembers having seen this hyaline fibroid appearance in the coats of the vessels of the cirrhotic kidney, unless where the organ had been badly prepared, or where the vessel was waxy. The small arteries, in this disease, are more frequently waxy than might be suspected. The drawings given by the authors in another paper (No. 192, xxviii. 1876-77, p. 361) of this hyaline substance in the spinal cord, carry with them the almost irresistible conviction that, in this locality at least, the hyaline substance is simply the colloid which forms in such abundance in the cords of quite healthy individuals when they are improperly preserved (see "Nervous System").

It was said by Johnson (No. 192, xxviii. 1876-77, p. 381) and others, that the hyaline appearance described by them was the effect of the media in which the preparations had been mounted.

Literature on Arterio-Capillary Fibrosis.—**Atkins**: Brit. Med. Journ., 1875, i. p. 445. **Dickinson**: Diseases of the Kidney, 1877, Part II. p. 536. **Galabin**: On the connection of Bright's Disease with Changes in Vascular System. **Gull and Sutton**: Med. Chirurg. Trans., lv. 1872, p. 273; Trans. Path. Soc., xxviii. 1876-7, p. 361. **Johnson**: Trans. Path. Soc., xxviii. 1876-77, p. 381. **Stewart (T. G.)**: Brit. Med. Journ., 1873, ii. p. 277.

Hyaline Degeneration.

594. The morbid condition which goes by this name, affects small arteries, capillaries, and, it is also said, minute veins (Wieger). It consists in the development of a translucent substance closely resembling the amyloid within the coats of the vessel, or in the immediate surroundings of the latter. The vessels become constricted, and the circulation through them is impeded or entirely suspended.

Öller (No. 13, lxxxvi. 1881, p. 329) has given a very careful description of the disease, as it occurs in the vessels of the retina, choroid, and optic nerve. He regards it as an endarteriitis which, in course of time, terminates in obliteration. The material is effused in nodular masses between the endothelium and perithelium of the capillaries, accumulates here, and by its bulk and elasticity compresses the channel. He traces its source to a degeneration of endothelial cells and extravasated coloured blood discs. The latter degenerate first. It makes its appearance in the arteries between the intima and elastic lamina, and causes atrophy of the media. The elastic lamina becomes wasted, and from the narrowing of the lumen of the vessel, caused by the pressure of the substance, a widespread thrombosis of the affected vessels ensues. The thrombus may itself subsequently become hyaline, a transformation which has also been described by Meyer (No. 4, vii. 1880, p. 598) in the clots filling aneurisms of the pulmonary, popliteal, and other arteries. The altered wall of the vessel and the hyaline thrombus, under such circumstances, constitute a continuous hyaline cylinder (see also Obermüller, No. 334).

Whether the hyaline fibroid state of the vessels described by Gull and Sutton (No. 34, lv. 1872, p. 273) in the arteries and capillaries of the kidney and other organs, in chronic interstitial nephritis, is similar to this, may be questioned. The hyaline degeneration under considera-

tion, forms nodular deposits along the course of the vessels, a condition quite different from that described by them.

Chemical Nature.—Although closely allied to amyloid in physical properties, the hyaline in question does not give its reactions with iodine, etc. According to Wieger (No. 13, lxxviii. 1879, p. 31) it remains diaphanous, shining, and intensely refractile on being treated with water or salt solution, and shows no swelling. Iodine solution gives a straw yellow colour, never a brown reaction. It is not dissolved by ether or chloroform, and mineral acids clarify it. It has a great tendency, in lymph glands at least, to calcify. He supposes that it is closely related to *elastin* in composition.

Literature on Hyaline Degeneration of Vessels.—**Arndt:** Arch. f. path. Anat., xl. 1867, p. 461; xlix. 1870, p. 367. **Cornil:** Journ. de l'anat. et de la physiologie, xv. 1878, p. 358. **Meyer:** Arch. d. physiol., vii. 1880, p. 598. **Neelsen:** Arch. d. Heilk., 1876, p. 119. **Obermüller:** Ueber hyaline Thrombenbildung, etc., 1886. **Öller:** Arch. f. path. Anat., lxxxvi. 1881, p. 329. **Thoma:** Arch. f. path. Anat., lxi. 1877, p. 227. **Wedl:** Sitzungsberichte. d. k. k. Akad. Wien., xlviii. 1863, p. 386. **Wieger:** Arch. f. path. Anat., lxxviii. 1879, p. 25.

Wax-like Disease.

595. When an organ or tissue is about to become waxy, it is in the small arteries and the capillaries that the first vestiges of the deposit are recognisable (see Sect. 126). The large arteries and veins usually escape. It differs from the hyaline degeneration of vessels in the nature of the substance which occasions the glass-like appearance, and also in the fact that this is an infiltration while the hyaline is a degeneration.

Healing of Arteries (see Chap. xix.)

Literature on Healing of Arteries.—**Ballance and Edmunds** (Experimental): Lancet, 1886, i. p. 922. **Burdach:** Ueber den Senftlebenschen Versuch. etc., 1885. **Lee:** St. George's Hosp. Rep., iii. 1868, p. 31. **Pfitzer:** Arch. f. path. Anat., lxxxvii. 1879, p. 397. **Pick** (Endothilium in): Ztschr. f. Heilk. Prag., vi. 1885, p. 459. **Raab:** Arch. f. path. Anat., lxxv. 1879, p. 451. **Schultz:** Ueb. d. Vernarbung v. Arterien. etc., 1877. **Senftleben:** Arch. f. path. Anat., lxxvii. 1879, p. 421. **Thoma:** Arch. f. path. Anat., xciii. 1883, p. 443; xcv. 1884, p. 294; civ. 1886, p. 209 *et seq.* **Virchow** (Closure of Arteries): Arch. f. path. Anat., vi. 1853, p. 583. **Warren:** The Healing of Arteries after Ligature in Man and Animals, N. Y., 1886.

Simple Fatty Degeneration.

596. In old people, in persons who are the subjects of pernicious anæmia, in individuals poisoned by phosphorus, and sometimes in young and apparently otherwise healthy persons, the small arteries and the capillaries of the brain, and, with less frequency, those of other organs, become fatty. The brain is the most typical *locale* of the degeneration.

It does not seem to be preceded by an inflammatory thickening of the vessel wall, but appears to be a purely degenerative change. The

muscular coat and the nuclei of the capillary walls suffer first. The whole vessel subsequently assumes, when examined microscopically, a uniform black colour from the aggregation of oil globules in its wall.

It is often a cause of cerebral or cerebellar hæmorrhage.

THROMBOSIS.

597. Definition.—As previously defined (Sect. 206), *A thrombus is a clot locally produced within the heart or a blood-vessel.*

The vessel may be either an artery or a vein. In the one case, it is known as an arterial thrombus, in the other, as a venous.

Localities.—The *veins of the calf of the leg*, the trunk of the

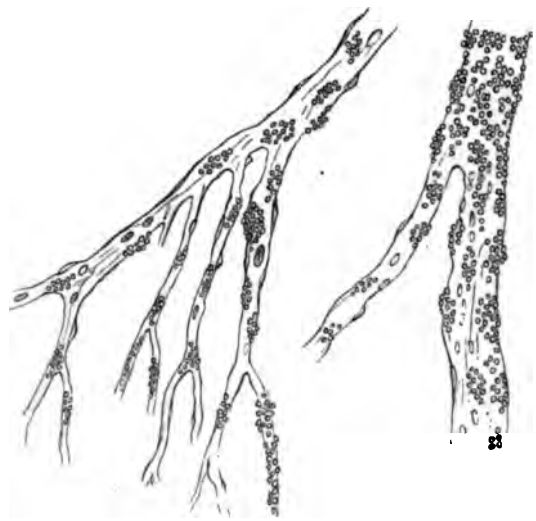

FIG. 200.—SIMPLE FATTY DEGENERATION, CAPILLARIES OF BRAIN (×300 DIAMS.)

saphena interna and its larger subdivisions, the *femoral*, the *vena cava*, the *portal vein*, and the *pulmonary artery*, are perhaps more often thrombotic than other vessels. Several instances of complete obliteration of the ascending vena cava have been recorded by Moullin, Warren, and others (see Bibliography); and even the *aorta* has been found closed by an adherent thrombus (Jaurand, Meynard, and others).

When the *cava* is occluded, the return of blood takes place by the azygos veins and those of the trunk which lie superficially. They consequently become much enlarged.

The portal vein has frequently been found totally or partially obstructed by an old firm thrombus (Stewart, Jastrowitz, and many others). If an obliteration limited to certain of its larger subdivisions should occur, the capillaries attached to those which are still pervious

become much distended, so as, in parts, to produce a characteristic nutmeg-like appearance, limited to certain areas of the cut surface. The appearance microscopically, is almost like that of an angeioma, so distended are the pervious capillaries. This resemblance is rendered still more striking from the fact that the liver cells intervening between these cavernous capillaries disappear from atrophy.

It is often stated that when the portal vein is occluded, the organ becomes cirrhotic. In some cases (syphilitic ?) the cirrhosis may have been really the cause of the thrombosis, not its effect; but in others it is probable that the toughness of the organ merely from capillary distention, may have simulated a new growth of fibrous tissue.

Diabetes mellitus is a common effect of occlusion of the portal vein, on account of the blood derived from the intestine, loaded with sugar, being returned by anastomotic paths into the general circulation without passing through the liver.

Thrombosis of the femoral vein and superficial veins of the thigh causes great swelling of the limb from œdema (phlegmasia dolens). When widespread, the thrombosis is usually the result of a phlebitis.

Formation and Organisation.—These have already been described in Chap. xix.

Terminations.—If the thrombus is of a septic nature, it is liable to disintegration, its fragments being carried with the blood current into distant organs. At other times it becomes bodily detached, and is transported into the right heart and pulmonary artery. If of large size, it will probably catch at the primary bifurcation of the artery, but if smaller, will be conveyed into the lung (see Infarction). It may be of such a shape that it does not completely fill the channel of the vessel in which it catches. The obliteration, in course of time, however, becomes complete by fresh clot being precipitated around it.

The thrombus, on the other hand, may retain its hold upon the vessel within which it was originally moulded. It will most likely organise subsequently or become calcareous. Where organisation takes place, the obliteration need not be complete, and, in the case of an arterial thrombus, it is often not so. Bands of organising tissue are pushed into the thrombus and coalesce at points, while the intermediate soft thrombus tissue is washed away, thus leaving a series of pervious channels through which the blood again circulates. The vessel, in such cases, appears, on cross section, to be provided with several lumina.

General Literature on Thrombosis.—**Alexander** (Portal Vein): Berl. klin. Wochnschr., iii. 1866, p. 35. **Baumgarten** (Review): Berl. klin. Wochnschr., xxiii. 1886, p. 385. **Botkin** (Portal Vein): Arch. f. path. Anat., xxx. 1864, p. 449. **Dickinson** (Portal Vein): Trans. Path. Soc., xiv. 1863, p. 63. **Eberth and Schimmelbusch**: Arch. f. path. Anat., ciii. 1886, p. 39; Fortschr. d. Med., iv. 1886, p. 581; Arch. f. path. Anat., cviii. 1887, p. 359; Fortschr. d. Med., v. 1887, p. 161. **Hanau**: Fortschr. d. Med., iv. 1886, p. 385; *Ibid.*, v. 1887, p. 65. **Hayem**: Rev. Scient., xxxii. 1883, p. 82. **Heucking**: Ueb. d. Organisation d. Thromb., 1886. **Jastrowitz** (Portal Vein, Syphilis): Deut. med. Wochnschr., ix. 1883, p. 682. **Jaurand** (Thromb. and Obliteration, Thoracic Aorta): Progrès méd., x. 1882, p. 147. **Leroux** (Portal Vein): Gaz

méd. de Paris, 1879, p. 332 *et seq.*; *Ibid.*, 1880, p. 372. **Leyden** (Portal Vein): Berl. klin. Wochnschr., iii. 1886, p. 35. **Löwit**: Deut. med. Ztng., vii. 1886, p. 930. **Mahomed** (Pulm. Art.): Trans. Path. Soc., xxxiv. 1882-3, p. 72. **Meynard**: Étude sur. l'obliteration de l'aorte abdominale, etc., 1883. **Moullin** (V. cava): Lancet, 1884. i. p. 390. **Osler**: Brit. med. J., 1886, i. p. 917. **Raymond**: Dict. encycl. d. sc., méd., xvii. 1887, p. 376. **Schimmelbusch**: Ueb. Thrombose im gerinnungsfähigen Blute, 1886. **Solowieff** (Portal Vein): Arch. f. path. Anat., lxii. 1874, p. 195. **Steven** (Innominate Art.): Glas. Med. J., xxi. 1884, p. 127. **Stewart** (Portal Vein): Ed. Med. J., xiv. 1869, p. 589. **Warren** (V. cava): Tr. Acad. Med. Ireland, i. 1883, p. 154. **Weigert** (White Thrombus): Fortschr. d. Med., v. 1887, p. 193. **West** (Portal Vein): Trans. Path. Soc., xxix. 1878, p. 107; *also* (Obliteration Coronary Art. Sudden Death), Trans. Path. Soc., xxxiv. 1882-3, p. 66.

EMBOLISM, PYÆMIC ABSCESS, AND INFARCTION.

598. **Definition of term Embolus.**—*A thrombus, or part of it, or any foreign body, carried along in the arterial circulation and impacted in a terminal branch. The act of impaction is known as embolism.*

Characters of Emboli.—They are most often vegetations or portions of vegetations detached from the cardiac valves, pieces of cardiac, venous, or arterial clot, calcareous scales, or globules of oil or air.

Septic Emboli are frequently implanted in the lung or other organ. They are oftenest located in the lung because it receives them at first hand from the veins; but the organisms contained in them appear to be capable of being carried through the lung and of gaining the arterial side of the circulation. They then either directly affect the organs to which they are transferred, or induce a malignant endocarditis which acts as a secondary source of contamination.

General Literature on Embolism.—**Bernard** (Incomplete Circulation of Bodies introduced into Vessels): Compt. rend. Soc. d. biol. **Changarnier**: Rec. d'ophth. Par., viii. 1886, p. 424. **Hamilton**: Liverpool Med. Chir. Journ., iii. 1883, p. 161. **Hirschberg**: Centralbl. f. prakt. Augenh., ix. 1885, p. 353. **Kirkes**: Edin. Med. and Surg. Journ., lxxx. 1853, p. 119. **Langton** (Multiple E. followed by Aneurisms): Proc. Roy. M. and Chir. Soc., Lond., ii. 1885-6, p. 153. **Minella** (Pulmonary): Gazz. med. di Torino, xxxvii. 1886, p. 337. **Raymond**: "Embolie," Dict. encycl. d. sc. méd., xxxiii. 1886, p. 605. **Thomson**: Journ. Am. M. Ass., Chicago, vii. 1886, p. 92. **v. Recklinghausen** (Venous) Arch. f. path. Anat., c. 1885, p. 503. **Virchow**: Ges. Abhandl. z. wissensch. Med., p. 219, 1862.

PHENOMENA FOLLOWING IMPACTION OF SEPTIC EMBOLI—PYÆMIA.

599. When a septic thrombus is detached and driven into an artery, it first of all acts mechanically in obstructing its channel. The micro-organisms which have been conveyed along with it begin to multiply and find their way through the coats of the vessel into the adjacent textures. They stimulate these to such an extent, that an inflammatory effusion is shortly afterwards poured out. In the case of the lung, the effusion resembles that of croupous pneumonia, but is confined to particular sharply isolated areas. It usually occurs towards the surface of the lung, because the embolus catches in a peripheral vessel.

The infiltrated patch of lung has a wedge shape and a well defined border. It is, at first, reddish in colour, but soon becomes gray or grayish-yellow. The solid exudation breaks down, becomes purulent,

FIG. 201.—PYÆMIC ABSCESS OF LUNG (×350 DIAMS.)

(a) Walls of alveoli; (b) effused small round cells; (c) fibrin lying in alveolar cavities; (d) cell entangled in meshes of same; (e, e, e) masses of micrococcus (staphylococcus) lying in the exudates (Gram's method of staining).

and is converted into a slough. In the formation of this slough, not only the exudation but the walls of the infiltrated air vesicles participate. An abscess-like cavity results, with shreds of half liquefied lung tissue within it,—a **pyæmic abscess** as it is called.

The contents of such cavities are pus corpuscles, more or less disin-

tegrated, shreds of tissue, and multitudes of micrococcus (staphylo- and streptococcus).

They are commonest in the lung, spleen, kidney, liver, and brain, and around joints.

It was Kirkes (No. 34, xxxv. p. 281; No. 19, lxxx. 1853, p. 119) and Virchow who discovered the embolic origin of pyæmic abscesses. Virchow's chief work on the subject is contained in his *Gesammelte Abhandlungen zur wissenschaftlichen Medicin*, p. 222. He showed, among other things, that if animal or elder pith emboli, substances which must have been contaminated with the germs of putrefaction, were introduced into the pulmonary artery circulation, they caused sloughy abscesses identical with those seen in pyæmia (p. 293). It sometimes happened that solid caoutchouc emboli could be similarly introduced without this effect, a difference which we now know might have been explained by their not having been contaminated with disease germs.

Literatre on Pyæmia.—**Bennett** (Report on the Effects of Pus in the Blood): Month. J. M. Sc., Lond. and Edin., xvi. 1853, p. 272. **Lee**: Med. Times and Gaz., vi. 1853, p. 105; *also*, Med. Press and Circ., xiv. 1872, p. 2. **Paget**: Lancet, ii. 1886, p. 203.

PHENOMENA FOLLOWING THE IMPACTION OF ASEPTIC EMBOLI—INFARCTION.

600. Old vegetations on the cardiac valves, calcareous scales, etc., are often of an aseptic nature, or, at any rate, if they contain micro-organisms, these have not the power of inducing a sloughy abscess. If they are carried into an organ or tissue, their effect depends upon whether the circulation within the embolised part is terminal or not.

By a **terminal artery** is meant one whose branches inosculate only with those of the corresponding vein, one which is devoid of collateral anastomosis. Such are the **renal** and **splenic arteries,** and, in a less complete manner, those of the **brain, heart, stomach,** and **lung.**

When an embolus is impacted within a branch of either the renal or splenic artery, the part necroses and becomes converted into what is known as an infarction. When, on the other hand, an embolus finds its way into any of the other above-mentioned arteries, it may not occasion any ulterior effect, or the necrosis it induces may be only partial.

v. Recklinghausen (No. 13, xx. 1861, p. 205) relates a case where a *thrombus* of the renal artery resulting from injury, gave rise to a yellow infarction of the organ within eight days.

On account of the kidney and spleen being so frequently the seat of infarctions, it is often supposed that emboli are driven into their respective arteries in preference to those of the limbs. That cannot be so; the embolus will certainly run more readily in a straight line than it will pass off at a right angle. The true explanation of their apparent preference for the kidney and spleen is, that,

when impacted here, the embolus leaves a permanent record of its existence in an infarction. When, on the contrary, it is driven into a texture such as a muscle, the anastomosis is so free that the tissue supplied by the occluded vessel does not die.

The term **Infarction** (*infarcire*, to stuff or cram into) was given by Lænnec (No. 335) to those wedge-shaped hæmorrhagic masses in the *lung* so often associated with valvular disease of the heart, on the understanding that the part was filled or stuffed with effused blood. In later times, it has been taken for granted that the wedge-shaped masses of necrosed tissue found in the *kidney* and *spleen*, often co-existently with the former, are also due to the part being distended with effused blood, and hence they are commonly named *hæmorrhagic infarctions*. This view, as well as the supposition that the hæmorrhagic infarct of the lung is due to embolism, seems to the author to be erroneous. The grounds on which this opinion is based will, however, be better understood after the detailed description of infarctions of various organs has been given.

INFARCTION OF THE KIDNEY.

Anatomical Characters.—It usually occurs in an individual with old or recent endocarditis accompanied by a growth of vegetations. Indications will be found of some of the latter having become detached, and if the renal artery be slit up carefully, one or more of them will probably be discovered in the branch or branches which formerly supplied the parts now in a state of necrosis.

On removing the capsule, depressed and sharply circumscribed areas of a pale cream-yellow colour will be noticed, which correspond to the seat of the infarctions. When cut into, the infarct has a wedge shape, the narrow end pointing to the hilus. Its general colour is pale cream-yellow, sometimes inclining at the border to an orange tint. In some instances a zone or fringe of a dark red colour is seen at its margin, but this "red zone," as it is named, is not so frequent in infarctions of the kidney as in those of the spleen. It is usually most evident towards the point of the wedge. The infarction feels tough and hard, and not a drop of blood can be squeezed out of it.

Question of Hæmorrhage.—These are the characters that the renal infarct usually presents. Is there a hæmorrhagic stage previous to this?

A slightly congested block of tissue is occasionally encountered in the kidney or spleen, but never, so far as the author's experience goes, is there a stuffing or cramming of the part with extravasated blood such as is met with in Lænnec's hæmorrhagic infarct of the lung. On the contrary, a quite recent infarction of the kidney or spleen is often paler than its surroundings. Nor is there tumefaction of the part such as is seen in the infarct of the lung—evidence of blood having been poured into it.

Examined microscopically, the outlines of the tubes, Malpighian bodies, etc., in the **strand of dead tissue** are seen to be preserved distinctly enough, even where it has a yellow colour. These are all, however, extremely granular; there has been a precipitation of albumin within it—a coagulative necrosis. Later on, it becomes caseous, and the outlines of its elements are consequently blurred.

The **red zone** is a zone of reaction. The vessels within it are engorged, and many of them will be found to have ruptured. Within it, there is thrown out in course of time a little cicatricial tissue. The dead piece of kidney substance becomes absorbed from the margin inwards, and as its removal is taking place the **cicatrix** in the reactive zone contracts. A little calcareous matter is sometimes left after absorption of the dead tissue has been completed, and this finally becomes embedded in the cicatrix. The cicatrix is depressed, and where several such cicatrices are found over the surface of the kidney or spleen, their cause ought to be of easy interpretation, more especially if associated with evidence of old endocarditis.

The author, however, does not wish to be understood as asserting that the vessels of the infarct are bloodless in all cases. What he wishes to emphasise, is that there is not a wide-spread extravasation of blood as in the hæmorrhagic infarction of the lung. It is rare even to find any unusually great turgescence of the vessels in the case of either the spleen or kidney.

Litten (No. 336) coincides in the above view, and Ziegler (No. 337, p. 66), although believing in their hæmorrhagic origin, has examined recent infarcts in which he was unable to demonstrate either hæmorrhage or its traces.

The common notion, that the renal infarct is a mass of hæmorrhage, was reiterated by Cohnheim (No. 338, p. 75); "As a fact," he wrote, "we constantly see as a result of embolism in the spleen, lung, and kidney, a hæmorrhagic infarction, whose description is a broad dark red triangular mass projecting over the neighbouring surface, base to periphery, apex to hilus."

Such a mass is often seen in the lung but not in the spleen or kidney; and, as will be shown, when it is present in the lung, it is usually not due to embolism but is simply and purely a hæmorrhage resulting from rupture of the distended capillaries of the organ.

Cause of Congestion.—If congestion of the piece of kidney tissue does follow, it is due, as Litten showed (No. 336), to the anastomotic vessels pouring their blood through the capsule, into the part deprived of its natural blood-supply.

Cohnheim (No. 31, i. p. 167) supposed that it was caused by venous regurgitation. This was disproved by Litten (*loc. cit.*) showing that, when the renal artery and vein are both ligatured, the kidney still becomes engorged.

INFARCTION OF THE SPLEEN.

The above description will almost literally hold good for the infarction of the spleen. There is usually a better marked red zone, in

which quantities of blood pigment are to be found. When the infarction is absorbed it leaves a cicatrix as in the kidney.

INFARCTION OF THE BRAIN.

Heubner (No. 327) and Duret (No. 4, 1874, p. 60) showed, by means of their beautiful injections, that the superficial vessels of the

FIG. 202.—EMBOLIC INFARCT OF SPLEEN (×40 DIAMS.)

The pale half of the figure represents the infarct. (*a*) Empty sinuses of spleen; (*b*) the infarct itself; (*c*) pigment around it; (*d*) splenic sinuses in neighbouring tissue; (*e*) a trabecula (Bismarck brown and Farrants').

brain, those which ramify in the pia mater, have a free anastomosis, but that the deep perforating twigs, which penetrate to the basal ganglia and capsules through the perforated spaces at the base, are completely terminal.

The effects of occlusion, by an embolus, of the main trunk of a cerebral

artery will vary, therefore, according as its deep or superficial branches are blocked. If the former alone, the cortex and superficial white matter may not suffer at all, or may necrose only partially. If the embolus, however, has closed the deep perforating branches, the parts supplied by them will certainly necrose.

The affected part becomes fatty, and compound granular corpuscles gather within it in abundance. Minute punctiform extravasations may be noticed at its border where the surrounding vessels have given

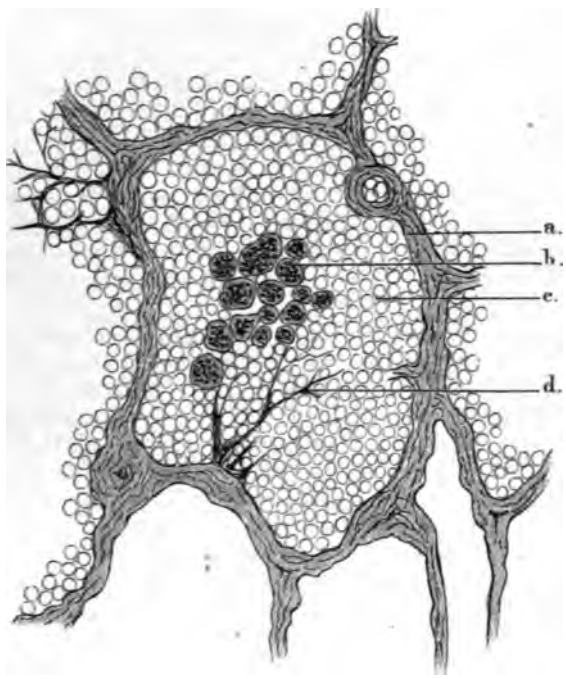

FIG. 203.—HÆMORRHAGIC INFARCT OF THE LUNG (×300 DIAMS.).
(*a*) Alveolar walls; (*b*) desquamated epithelium containing pigment; (*c*) effused blood corpuscles lying in an air vesicle; (*d*) band of fibrin (Picro-carmine and Farrants').

way in the endeavour to establish anastomosis. The part, in course of time, may be entirely absorbed.

HÆMORRHAGIC INFARCTION OF THE LUNG.

Anatomical Description.—It is found in connection with valvular disease of the heart, more usually with mitral than with aortic. Co-existently with it, there may be yellow infarctions in the spleen and kidney. The lung infarcts are commonly multiple, have a wedge shape when adjacent to the pleura, and are rounded when

located near the root. They vary in size, some being minute, almost punctiform, while others may possess a base of an inch and a half to two inches. The mass projects so much above the surface as to constitute a prominent object even before the part is incised. It is hard and tough, with a well defined sharp border, and has a leaden or purple colour when seen through its pleural covering. On cutting into it, the wedge shape is usually very striking, and the colour is almost black from the deeply venous hue of the blood contained within it. The lung tissue is generally much congested, and patches of brown induration may be seen here and there.

The mass is composed, according to its size, of a group of air vesicles or lobules filled with blood. The blood lies in the cavities of the air vesicles, not in their interstices. The latter present a compressed appearance. Cohnheim stated that the effused blood does not contain fibrin. This is not so. A rich fibrinous network can often be detected within the air vesicles. The hard pneumonic feeling of the mass would indicate that the effused blood had coagulated. There is no evidence of necrosis of the piece of lung tissue implicated. Large half-crystalline masses of hæmoglobin separate soon after the hæmorrhage has occurred.

Although these hæmorrhagic infarcts may be numerous, there is nothing to show that they necrose, as the embolic infarcts of the spleen and kidney do. There are no cicatrices to indicate the presence of former effusions. Some of them may be partially decolorised and softer than the others, but they do not become cheesy as in the case of the embolic infarcts of the spleen and kidney; nor do they slough to constitute pyæmic abscesses, unless where they are of septic origin. The blood, in fact, is simply absorbed shortly after being poured out, and leaves the lung tissue vesicular and unimpaired.

Cause.—The usual supposition is that these hæmorrhagic foci are embolic. This was not the original idea entertained of them by Lænnec, and there is a good deal of truth in what Cornil and Ranvier remark (No. 255, i. p. 514), that since the doctrine of embolism has become generalised "there has been a certain tendency in science to refer to embolism all that the older writers called infarctus."

The reasons which have led to this supposition are (1) that the foci are found associated with valvular disease of the heart; (2) that wedge-shaped embolic infarctions are often seen to be co-existent with them in the spleen and kidneys; and (3) that they have a wedge shape and are located close to the periphery of the organ.

If they are embolic, where do the emboli come from? The usual answer is that the blood, in valvular disease of the heart, has a tendency to coagulate on the right side of the circulation, and that portions of the clot are driven into the pulmonary artery. This statement is founded on nothing more than theoretical grounds—theory of the most unwarranted character. It has never been shown that the blood in heart disease has more tendency to coagulate within the vessels than in a

host of other diseases unassociated with pulmonary infarction; and emboli, moreover, cannot be discovered on dissecting up the vessel leading to the affected part.

Virchow found (No. 129, pp. 285-294) that aseptic caoutchouc emboli introduced into the right side of the circulation through the jugular vein, did not occasion in the dog any particular change when they became impacted in the lung.

Panum (No. 13, xxv. 1862, p. 452) made out that small simple emboli placed within the pulmonary artery merely become encapsuled, and induce no further change in the lung tissue. Cohnheim (*loc. cit.*) and Litten (*loc. cit.*) verified these results with emboli composed of paraffin.

FIG. 204.—SECTION OF AN ALVEOLUS FROM LUNG OF A PERSON WHO DIED FROM MITRAL DISEASE (× 350 DIAMS.)

(*a*) Distended and projecting alveolar capillaries; (*b*) desquamated epithelium; (*c*) blood-corpuscles extravasated into alveolar cavity (Picro-carmine and Farrants').

When a thrombus is driven embolically into the lung from a vein in Man, it does not cause a hæmorrhagic infarction, but the part, being deprived of blood, becomes peculiarly anæmic; nor does fat embolism lead to it.

Conclusions.—The conclusion, therefore, seems inevitable, that in by far the greater number of instances of hæmorrhagic infarction of the lung, the effusion has nothing to do with embolism.

It is caused simply by one or more of the capillaries of the lung, in a state of chronic distension from the valvular disease, rupturing.

The wedge shape is due, not to the distribution of the terminal branches of the pulmonary artery, but to the shape of the terminal bronchus and attached air-vesicles in which the blood is confined.

Hæmorrhage into the lung from any cause (rupture of an aneurism, *e.g.*) will assume a wedge shape for the above reason, if located near the periphery.

Coloured injection driven into the air-vesicles by piercing them with a sharp cannula through the pleura assumes exactly the same wedge shape. Figure 205 represents an artificial infarction so produced.

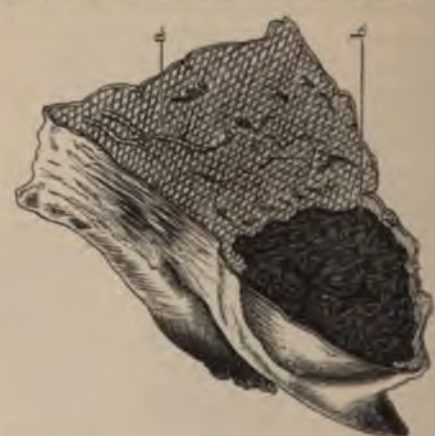

FIG. 205—ARTIFICIAL INFARCT OF LUNG MADE BY INJECTING PRUSSIAN BLUE INTO THE AIR VESICLES.

(*a*) Lung tissue free from injection; (*b*) wedge-shaped injected mass (natural size).

GENERAL CONCLUSIONS ON SUBJECT OF INFARCTION.

1. The infarctions of the spleen and kidney are due to the blood-supply being cut off from the part, and the most common source of this is embolic plugging of the respective arteries.

2. They are not usually accompanied by hæmorrhage unless in the zone of reaction which surrounds them, although congestion and punctiform extravasation are possibilities in the early stages.

3. They are veritable necroses, the necrotic changes within them resembling those which follow the total removal of the blood supply in other protected parts of the body.

4. They are absorbed in course of time, and the formation of a depressed cicatrix follows.

5. Embolism of the arteries of the brain is accompanied by a similar necrosis, but, as the arteries of the encephalon are terminal only in certain regions, the necrosis of the part supplied by an occluded artery is never so wide-spread as in the case of the spleen and kidney.

Hæmorrhages may occur here owing to the attempt to nourish the part by collateral channels, and to the softness of the surroundings.

6. The hæmorrhagic infarction of the lung is simply an apoplexy due to various causes. By far the most frequent, however, is rupture of alveolar capillaries unduly distended by the regurgitant pressure resulting from valvular disease of the heart. Its wedge shape is caused by the shape of the bronchus and the air-vesicles in which the effused blood is contained, and not by the distribution of a terminal branch of the pulmonary artery. The lesion usually has nothing to do with pulmonary artery embolism, but a hæmorrhage from any cause, if situated at the periphery of the lung, will have the usual characters of a hæmorrhagic infarction.

7. The blood in these pulmonary infarctions is rapidly absorbed, leaving no trace of its former existence.

Literature on Infarction.—**Cohnheim:** Untersuch. üb. d. embolischen Processe, 1872. **Cornil et Ranvier:** Manual of Path. Histology, i. 1882. **Hamilton:** Liverpl. Med. Chir. Journ., iii. 1883, p. 161. **Herxheimer:** Arch. f. path. Anat., civ. 1886, p. 20. **Laennec:** Traité de l'auscultation. **Litten:** Untersuch. üb. d. haemorrhagischen Infarct., 1879. **v. Platten:** Arch. f. path. Anat., lxxi. 1877, p. 31. **v. Recklinghausen:** Arch. f. path. Anat., xx. 1861, p. 205. **Virchow:** Gesammelte Abhandlungen z. wissensch. Med., 1862. **Ziegler:** Text-book of Patholog. Anat., Trans. by Macalister.

FAT EMBOLISM.

601. **Definition.**—*A condition in which finely divided globules of oil are carried into the arteries and capillaries of the lung, brain, kidney, etc., and become impacted within them as embolic obstructions.*

Historical.—This remarkable form of embolism was discovered in the year 1862 by Zenker (No. 339, p. 31; also, No. 36, 1862, ii. p. 63) and Wagner (No. 126, iii. p. 241). There was much difference of opinion, at first, as to how the oil got into the vessels, but it is now known that it may be derived from various sources.

Sources.—The commonest of these is from the medulla of a fractured bone. The oil is evidently aspirated into the lacerated veins with great ease, and is thus transported to the lung. Rupture of a fatty liver (Zenker and Hamilton) may be another cause of it. The oil escapes into the rupture and is absorbed by surrounding vessels. It has been said that the oil derived from fatty degeneration of an abscess may also be a source of it. The lipæmic blood of diabetes (p. 530) has been shown to circulate with great difficulty (Sect. 448). The oil globules contained in it catch in the tortuous capillaries and arteries of the *lung* and other organs, and thereby obstruct the onflow of the blood (Sanders and Hamilton, No. 19, xxv. 1879, p. 47). In various other morbid states of the blood similar embolic occlusion of the vessels with oil has been found.

Anatomical Characters.—The lung is the organ in which they are always most abundant. The blood of the large pulmonary vessels

has often an oily appearance to the naked eye; while, microscopically, homogeneous masses of oil, staining black with perosmic acid, are seen to plug the terminal branches of the pulmonary artery. They are closely applied to the wall, and, as a rule, completely fill the channel, an indication that they must have been driven in by the *vis e tergo* exerted upon them by the column of blood.

Complete networks of capillaries upon the walls of the air-vesicles can often be seen choked with oil, so much so, that they resemble an artificial injection.

In lipæmic blood, the oil globules are more minutely sub-divided than where they have been derived from bone medulla. They are combined with a quantity of granular matter, and the two together effect a complete obstruction in the small arteries and in the capillaries.

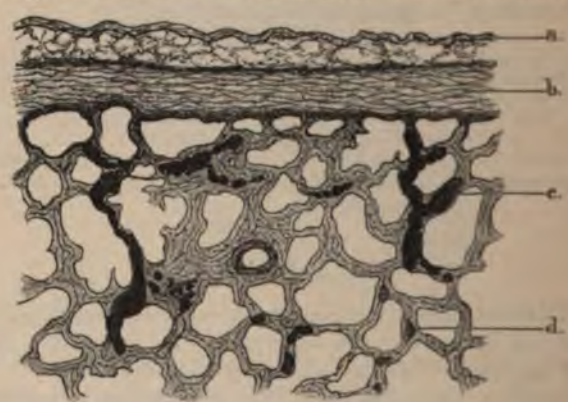

FIG. 206.—FAT EMBOLISM OF LUNG FROM FRACTURED BONE (× 50 DIAMS.)

(*a*) Superficial layer of pleura; (*b*) deep layer of pleura; (*c*) large embolus; (*d*) smaller capillary embolus (Perosmic acid and Farrants').

The oil sometimes manages to pass the lung, and is then found mostly in the tortuous small vessels of the *brain* and *kidney*. In the latter organ, it has most tendency to catch in the *Malpighian tuft* which is sometimes the only locality in which it may be discovered.

The vessels of other organs throughout the body become similarly impermeable, the extent to which they are influenced apparently depending on the tortuosity of their capillaries.

In some animals (dog and cat), the oil when artificially injected is excreted by the kidney, but it is questionable whether this ocurrs in Man.

The cause of the oil failing to circulate, is that it is of too light specific gravity (see Chap. xiii.)

Effects.—In the case of the lung, it occasions symptoms of impeded respiration, and in many cases ends fatally. It has been said that fat embolism of the lung occurs in all fractures of long bones, but that it

is only where the absorption has been excessive that it excites any symptoms.

Œdema of the lung, or croupous pneumonia, is frequently induced through the mechanical obstruction to the blood circulation, and the functions of the kidney are, as might be expected, seriously compromised.

Literature on Fat Embolism.—**Altdorfer**: Experimentelle Studien ub. d. Einfluss d. Oeles a. d. Blutcirculation d. Frosches. Greifswald, 1875. **Busch**: Arch. f. path. Anat., xxxv. 1866, p. 321. **Czerny**: Berl. klin. Wochnschr., xii. 1875, p. 593. **Flournoy**: Contrib. à l'étude de l'embolie graisseuse, Strassburg, 1878. **Sanders and Hamilton** (in Diabetes): Edin. Med. Journ., xxv. 1879, p. 47. **Jolly**: Arch. f. Psych., xi. 1881, p. 201. **Mansell-Moullin**: Intern. Encyc. of Surg., i. **Reiter**: Ueber Fettembolie. Würzb., 1886. **Scriba**: Deut. Ztschr. f. Chir., xii. **Virchow** (F. E. and Eclampsia): Deut. med. Wochnschr., xii. 1886, p. 488; *also*, Berl. klin. Wochnschr., xxiii. 1886, p. 489. **Wahncau**: Ein Fall tödlicher Fettembolie, 1886. **Wilks**: Brit. Med. Journ., 1883, i. p. 768. **Wiener**: Wesen u. Schicksal d. Fett. Emb., 1879.

AIR EMBOLISM.

602. Air is sometimes aspirated from a large open vein. If air be forcibly pumped into the lung, of an animal, it may cause rupture of the air-vesicles, be extravasated into the interstitial tissue, and be partially absorbed by the vessels. It is sometimes found in the chambers of the heart in such animals.

The danger from its gaining entrance to the circulation is extreme. It either causes instantaneous death, or greatly impedes the pulmonary circulation.

The cause of its failing to circulate along with the blood is the same as in fat embolism, namely, that it is too light.

ANASTOMOTIC ECTASY OF ARTERIES.

603. When the main trunk of an artery possessing anastomotic vessels is ligatured or otherwise obstructed, the latter soon dilate, and so continue the supply of blood to the part. The means by which the distension of the collateral channels is effected, is as yet not clearly understood. The current theories on the subject are mainly the following:

Weber (No. 115, i. Ab. i. p. 176) held that the blood-pressure above the point of ligature must be locally raised, and that this acts in dilating the anastomotic channels.

This theory is often alleged to be faulty in many respects. Any increase in pressure, it is said, must react over the whole circulation. Cohnheim (No. 31, i. p. 89 *et seq.*) asserted that, after the sudden ligature of a large trunk, such as the femoral in the dog, setting aside a slight rise at the time of occlusion, the pressure on the proximal side of the ligature, at the point of junction of the femoral and external iliac, or even in the external iliac itself, is just the same as that of the opposite artery.

He stated, rightly enough (*loc. cit.*, p. 92), that when a main trunk going to a limb

or other part is ligatured, the collateral vessels supplying that part alone dilate, not those supplying adjacent parts. Thus, if the right common carotid is tied, hyperæmia of the right arm does not ensue, but the vessels which dilate and which continue to carry on the circulation in the head, are the left carotid and the right vertebral. Similarly (p. 94), when one branch of an artery supplying an organ is obstructed, more blood enters those which are open. He concluded that the mechanism which effects this local dilatation must be bound up with the vaso-motor nerves.

Talma (No. 169, xxiii. 1880, p. 224) takes a different view of the matter, a view which goes to support Weber's theory. He says (p. 268) that the pressure can and does rise locally in an artery after ligature, without there being a general increase. The blood flowing into the arteries has, as a result of the systole of the heart, a certain amount of actual energy. If its movement is suddenly obstructed, a great portion of this energy must be converted into heat; part of it, however, will become potential, and this potentiality will tend to raise the pressure locally immediately above the point of ligature.

The larger the branch of an artery which is closed, the greater the increase of pressure in the trunk and in the collateral branches (*loc. cit.*, p. 269). If the arteria profunda femoris is ligatured while the femoral artery remains patent, the pressure within the latter is raised, and he holds that it is this over-pressure which causes

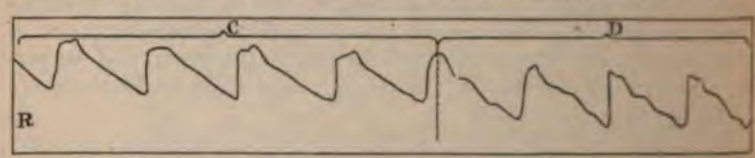

FIG. 207.—TRACING OF RADIAL PULSE TAKEN WITH THE DIRECT SPHYGMOGRAPH.

The first half, C, was during compression of the two femorals, the second half, D, when the pressure of the arteries was relaxed.

the collateral branches to dilate. He concludes (p. 274) that the regeneration of the circulation after ligature of an artery is effected on purely mechanical principles.

He (*loc. cit.*, p. 239) mentions that the lowering of the temperature of the part consequent upon the obstruction to the circulation might be supposed, reflexly, to bring about a dilatation of the collateral branches. His experiments, however, on this subject convinced him that this was incorrect, and that the restoration of the circulation through anastomotic paths cannot be explained by the agency of the vaso-motor nerves. Division of the sciatic, moreover, has little effect in hastening the flow of blood through the collateral channels after ligature of the main trunk.

According to the same author (*loc. cit.*, p. 264), the small branches dilate first, the large afterwards.

Marey (No. 346, p. 338) distinctly states that the general arterial tension also materially rises when an artery of considerable volume is compressed, because "by this means an important path for the passage of the blood into the venous system is suppressed. He represents it graphically in the accompanying sphygmogram (Fig. 207), taken from the radial when the two femorals were simultaneously compressed. The first half of the tracing was taken while the vessels were compressed, the second after the compress had been removed, the fall in pressure induced thereby being evident.

Compression of the aorta of the horse through the rectum, induces a still more evident rise in the general arterial tension.

Rapidity with which Circulation is Established.—When a

main vessel is ligatured the temperature of the part beyond at first sinks, but subsequently rises as the collateral circulation begins to be restored. It is usual to regard the anastomotic dilatation as being completed when it becomes again normal. This, Talma holds, is incorrect. The vessels go on enlarging for a considerable period afterwards.

If the crural artery be ligatured in a dog, and, after the temperature has become normal, both its paws be kept for some time in iced water, the one which corresponds to the side on which the artery had been occluded becomes gangrenous, the other does not, showing that the circulation at this period has not been thoroughly reinforced.

The rapidity, however, with which the collateral vessels may become dilated is perhaps greater than might be expected. Twenty-four hours after ligaturing the carotids in a horse, Marey and Chauveau (No. 346, p. 625) found that the small arteries were so distended that it was with difficulty they could perform tracheotomy, each small branch having to be tied.

The blood, moreover, takes the shortest route in completing the anastomosis.

VEINS—INFLAMMATORY AFFECTIONS—PHLEBITIS.

604. The chief forms of inflammation met with in veins are the exudative and suppurative.

In the **exudative** the wall becomes thickened and infiltrated with a small round cell deposit. Little granulation-like projections sprout out from the tunica intima, whereby it assumes a roughened appearance, and these are soon coated with fibrin. A thrombus, in course of time, blocks the channel, which becomes subsequently organised by the penetration of new tissue derived from the wall (see Sect. 210). The vessel may thus be rendered impervious.

The **suppurative** is commonly associated with a septic wound. The coats of the vessel become the seat of a purulent infiltration, which often constitutes an abscess cavity. This abscess cavity may dissect the coats asunder and perforate into the vessel by two or more openings. The blood can circulate temporarily through these, so that, after death, it often appears as if the vessel had two channels.

If a clot should be thrown down, it will usually be found to be of a greenish colour and loosely adherent to the wall of the vessel. When incised, it may present several abscess-like cavities (see admirable representation by Cruveilhier, No. 332, ii. 1835-42; Livr., xxvii. pl. 4).

As before described, this state of a vein is one of extreme danger from its liability to excite pyæmia. The interior of the vein and the softening clots may frequently be found to be covered with, or to contain, large quantities of micrococcus.

Literature on Phlebitis.—**Chamousset**: Quelques recherches sur la phlegmesia alba des nouv. accouchées, Thèse de Paris, 1873. **Chvostek** (Suppurative): Arch. gén. d.

méd., 1870, i. p. 229. **Cruveilhier** (various Forms): Anat. path. (see various References under Phlébite, Index, Vol. II.). **Fraentzel** (Suppurative) Berl. klin. Wochenschr., vi. 1869, p. 3. **Gross** (Suppurative): Am. Journ. med. Sc., cxxii. 1871, p. 337. **Gull** (Suppurative): Med. Chir. Trans., xxxviii. 1855, p. 157. **MacClintock** (Puerperal): Dub. Med. Journ., Aug. 1856. **Moutard-Martin** (Suppurative): Bull. de la Soc. anat., 1874, p. 848. **Playfair**: (Puerperal) Trans. Obstetric Soc. Lond., xvi. 1875, p. 62. **Robin** (Obliterative): Arch. de Physiol. norm. et path., i. 1874, p. 897.

FIG. 208.—ACUTE PHLEBITIS. SMALL BRANCH OF INT. SAPHENOUS (× 40 DIAMS.)

(*a*) Fat cells; (*b*) areolar coat infiltrated with fibrin; (*c*) muscular fibres cut across; (*d*) small-cell infiltration of wall; (*e*) intense small-cell infiltration of tunica intima; (*f*) laminated deposit of fibrin; (*g*) accumulated leucocytes on same (Hæmatoxylene and Farrants').

VARIX (PHLEBECTASY).

605. The term is applied to the irregular beaded dilatations so frequently seen in the course of veins in different localities. The chief seats of the disease are the veins of the leg and thigh, the plexus pampiniformis or the ovarian veins, the hæmorrhoidal veins, and occa-

sionally those of the abdominal wall. In addition to being irregularly dilated, the vessels become extremely tortuous. Thrombi are commonly found in their interior, and these have a tendency to calcify (phleboliths). Calcareous scales may also sometimes be found in their wall (Consult *Epstein. Arch. f. path. Anat.*, cviii. 1887, p. 239).

HÆMORRHOIDS—(See DIGESTIVE SYSTEM).

CHAPTER XLIV

THE BLOOD VESSELS—(*Continued*)

The Arterial Pressure in Health

606. The pressure of the blood within the arteries of the larger circuit is normally dependent upon the following factors :—

(1) The propelling power of the ventricle ;
(2) the quantity of blood driven into them ;
(3) the rapidity of the heart's beat ;
(4) the elasticity and contractility of the tissues ;
(5) the amount of impediment offered to the passage of blood from their outlets ;
(6) the influence of respiration.

The **first** and **second** of these items together, of course, represent the momentum with which the blood will be emitted from the heart. The quantity may be large, but the propelling power weak, as where the ventricle is dilated but not hypertrophied ; and this might possibly not have so much effect in maintaining the arterial pressure as where the quantity is smaller but the propelling power more vigorous.

A dilated ventricle without hypertrophy would require relatively more inherent contractility in order to empty itself than one of natural size, owing to the mass of blood being greater.

In regard to the **third** item, it must be remembered that the work done by a ventricle is by no means proportionate to the *rapidity* of its contractions. In fact the reverse seems rather to hold good. A small number of vigorous contractions within a given time, in reality, exert a greater influence in propelling the blood than a large number of contractions which are feebler.

The increased energy with which the blood is propelled, moreover, must not be confounded with a necessary rise in *arterial pressure*. Arterial pressure is dependent upon so many factors that the abasement or annihilation of one may often more than counteract increased vigour in another. With the slackening in the rapidity of the heart's beat

the arterial tension *falls*, and the arterial oscillations, as shown by tracings, become more ample.

Marey (No. 346, p. 187) explains this phenomenon by there being more time afforded in slow pulsation for the blood to leave the arteries and to pass into the capillaries, than where the pulsations follow each other rapidly. The artery consequently becomes relaxed, while the following systole, driving a mass of blood into the loosely distended vessel, occasions a tracing of great amplitude. The quantity of blood which is ejected from the heart will also be greater, because it has had time to accumulate within its chambers.

Conversely, when the cardiac contractions increase in frequency the amplitude of the tracing diminishes, the reason being that the artery is kept on the stretch, and does not recoil so much as in the former case.

It will be necessary to explain that under the **fourth** item the elasticity of the arterial walls is included along with that of the tissues generally. The reasons for this have already been given in Section 551.

Instead of viewing the elasticity and contractility of the arteries as the only obstacles to their becoming dilated by the pumping action of the heart, we must take into the reckoning the total elasticity of the tissues, vessels included.

The mechanism of the dicrotic wave of the pulse, the production of dicrotism in disease, the dilatation of the ventricle in aortic regurgitation (see p. 629) will, therefore, have to be held as not dependent upon the elasticity of the arteries alone, but as bound up with that of the whole tissues.

The **fifth** item specified as concerned with the arterial pressure is pathologically a most important one. The passage of the blood out of the arterioles may be hindered in several ways, one of the most important being of course the contraction of the muscular coat. This appears to be a condition present in several diseases accompanied by high arterial tension, and its relief conduces to the most beneficial results.

The free discharge of blood from the arterioles, however, may also be retarded by obstruction in the capillaries. The elasticity of the surrounding parts just referred to, will react upon the capillaries as well as upon the arteries, and although the former may possess but feeble contractile power in themselves, yet the blood may be seriously hindered in its transit by the recoil of the adjacent liquids and tissues. The pressure within the capillaries and within the arteries is probably just counteracted, or nearly so, in health, by that of the parts around them. In disease, it is capable of becoming much greater or much less.

When the arm is placed in a plethysmograph and surrounded with liquid, the slightest pressure above that of the arteries is sufficient to induce anæmia of the limb followed by complete arrest of the circulation.

Not only from this cause, but from others, such as a wrong composition of the blood, the forward movement of the blood-stream may be seriously hampered within the capillaries. Alterations in the specific

gravity of the plasma, as in Bright's disease, anæmia, etc., would tend to unsettle the regular onflow of the blood corpuscles (see Chap. xiii.), and would thus hinder their ready transmission from the arterial to the venous side of the circulation.

Respiration acts in a twofold manner. During inspiration the arterial pressure is lowered, while during expiration it is augmented.

The Pulse.

607. **What it is.**—The pulse consists in the sensation imparted to the finger when it is made to compress an artery. The impact of the blood-wave against the compressed vessel communicates the sensation; or, as Broadbent (No. 6, 1887, i. p. 655) expresses it, "It is the change of shape from the flattened condition impressed upon the vessel by the finger or sphygmographic lever to the round cylindrical shape which it assumes under the distending force of the blood within it."

A good deal of the sensation communicated to the finger must be due to the vibration of the liquids and tissues around the vessel. If the finger be laid over an exposed artery of large size such as the femoral or the aorta, only a feeble sense of pulsation is communicated to it. The liquids of the tissues surrounding the artery probably amplify the pulsation transferred to them, and hence render the pulse more apparent.

It must always be borne in mind that a sphygmographic tracing is not the tracing of the pulsation of the artery but of the tissues and liquids surrounding it.

Roy (No. 179, ii. 1879-80, p. 66) has recorded the curve of the exposed carotid of the rabbit by means of an instrument which he names the **sphygmotonometer.** He finds a number of secondary indentations on the descending part of the sphygmogram which he supposes may be due to vermicular contraction of the muscular coat. One of the chief objections to his experiments lies in the fact that the vessel (carotid) was tied and cut across, so that the record was not that of the blood in its continuity but under conditions of obstruction.

The rate of the pulse-wave must not of course be confounded with that of the transmission of the blood itself. For while the rapidity of the former has been estimated at something like 30 feet per second, the latter is at most only about $\frac{1}{18}$ to $\frac{1}{20}$ of this. The time occupied by the primary pulse wave in travelling from the heart to the foot in a man, is somewhere about $\frac{1}{6}$ second. It is propagated more rapidly when the arteries lose some of their elasticity, as when they become atheromatous. The conditions then approach more closely to those of a liquid within a rigid tube.

Pulse and Arterial Pressure.—A certain mean pressure is maintained in the arteries, which tends to drive the blood continuously through them and through the capillaries. The pulse is in great part the expression of each heart's systole over and above this. This mean pressure is the resultant of certain factors previously enumerated (p. 694). Were the heart to cease beating, the aortic valve to be closed, and the capillary outlets to be occluded simultaneously, the

pressure of the blood within the arteries would represent this mean pressure.

Each systole of the heart augments the arterial pressure for the time being and causes a greater or less increase in the diameter of the arteries. It is not this increase of diameter, however, which is felt by the finger, or which is recorded by the sphygmographic lever, but rather the impulse communicated by the wave when the artery is compressed. In order to fully estimate the character of the pulse a certain amount of pressure must be exerted. The finger simply laid over the site of the radial artery has no appreciable impulse communicated to it; nor can an ample sphygmographic tracing be obtained without the artery being compressed.

Sphygmogram no Test of Pressure.—The mean arterial pressure differs in individuals either as an idiosyncrasy, as a forerunner of impending disease, or as an effect of disease already present; and according to the amount of compression necessary to obtain a full sphygmographic tracing, or to entirely obstruct the circulation through the vessel, so the extent of the arterial pressure may be roughly gauged. The pressure required to occlude the artery is, however, much less than that of the blood within it, and hence merely a relative result can thus be obtained. The height to which the lever rises in the up-stroke is no criterion of what the arterial pressure actually is. It simply indicates the result of a more or less powerful ventricular contraction upon a relaxed or rigid set of arteries. A long and sudden up-stroke does not necessarily demonstrate that the heart is beating more powerfully than usual. It may be due to this cause, but is not always so, because a comparatively weak heart's contraction, such as that of a person *in articulo*, may induce a powerful pulse-wave, provided that the arteries have been relaxed previous to its taking place.

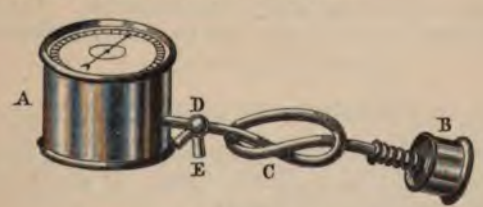

FIG. 209.—v. BASCH'S SPHYGMOMANOMETER.

Measurement of Arterial Pressure in Man.—The sphygmomanometer devised by v. Basch (No. 43, xxiv. 1887, p. 179) probably gives more accurate results than any other instrument in use at the present day. It consists of a hollow chamber or pelotte B, one end of which is covered with a delicate caoutchouc cap, the other connected with a flexible tube C, which is in communication with a metal manometer A. The manometer is constructed on the same principle as an aneroid barometer. The pressure is indicated by means of a

needle and index. The metal capsule of the manometer, the caoutchouc tube, and the pelotte are filled with water. A tap to assist in the filling of the instrument is placed at E.

The pelotte is adjusted over an artery which can be readily compressed against a resistant background—the radial by preference. It is then made to impinge upon the artery until the finger placed on the distal side ceases to recognise pulsation. The index shows the number of degrees through which the needle has traversed, each degree representing a pressure of 10 mm. Hg. The operator requires to have had much practice with the instrument before attaining to reliable results.

Pulse v. Ventricular Contraction.—The general belief is, as Marey remarks (No. 346, p. 282), that a strong pulse corresponds to an energetic ventricular contraction, and that a weak pulse is indicative of ventricular weakness. This is true of a small number of cases, but by no means of all. The pulse is strong or feeble according as the heart impels a full or a small wave into the arteries, and this is regulated in great part by arterial tension, that is to say, by the resistance offered.

Thus the feeble pulse of a patient in pneumonia does not necessarily indicate that his powers are at a low ebb, but rather that the arterial tension is high. The intensity with which a patient's arteries beat is, contrariwise, no indication of his reserve forces. Venesection relieves arterial tension, and hence its effect in restoring the pulse in pneumonia (Marey).

Different degrees of arterial tension alone may modify the pulse without the heart being at all concerned. It is, in reality, the state of contraction of the arterioles which mainly controls the extent of the resistance; and it does so by hindering the free passage of blood to the capillaries and to the venous side of the circulation. The more relaxed these are, the lower, *ceteris paribus*, will the arterial pressure be.

VARIETIES OF THE PULSE.

The older physicians placed much reliance upon the feeling communicated by the finger to the pulse. Some of the chief varieties recognised by them were the following.[1]

The *Ardent*, in which the pulse seems to raise itself to a point and strike the finger forcibly; *Bounding*, called also *Caprizans*; *Contracted*, narrow, deep, and rather hard; *Critical*, which after presenting the character of irritation, becomes open and soft; *Deep*, felt only by pretty strong pressure; *Developed*, broad, full, strong, and frequent; *Dicrotus*, having a double stroke; *Feeble*, striking the finger feebly; *Febrile*, generally implying sustained frequency; *Filiform* or *Thready*; *Formicans* (like the creeping of an ant), small and scarcely perceptible; *Frequent*, numerous pulsations in a minute; *Full*, the artery seeming distended (hard or soft); *Intercurrent*, in which,

[1] Compounded from Hooper (No. 341) and Copland (No. 342).

after several pulsations, one or more seem to break in abruptly; *Intermittent*, the pulse ceasing for one or more beats and then continuing, and so on alternately; *Irregular*, the pulsations varying in frequency or force; *Myurus*, a sinking pulse, the second stroke of which is less than the first, the third than the second, etc., the pulse thus diminishing like a mouse's tail; *Sharp* or *Jerking*, striking the finger sharply and suddenly; *Small; Soft; Tense; Vibratory*, etc.

It was also frequently described under the following groups of terms:—(1) Hard, resistant, tense, firm, or sthenic. (2) Contracted, constricted, or concentrated, and small. (3) Full, large, broad, ample, or open, and bounding, etc. (4) Soft, compressible, empty, weak, feeble, unequal, small. (5) Precipitate, quick, rapid, sudden, vibratory. (6) Languid, undulatory, etc.

They recognised a *pulsus frequens* and a *pulsus rarus* which, as Galabin puts it, "by some subtle sense, lost to the moderns, were differentiated from the pulsus celer and pulsus tardus." The same author also asserts that our old physicians never quite attained the skill in pulse feeling of which their Chinese colleagues boast, who pretend to distinguish upwards of three thousand varieties of pulse. He explains it by the Celestials having been much longer at the business than their occidental brethren!

The typical pulse of **fever** was described as *frequens, magnus* (voluminous) et *celer*, while that of **plethora** was held to be *magnus* et *tardus*.

A *feeble soft pulse* was generally recognised as associated with **general** or with **cardiac debility.**

The pulse of **incipient inflammations** was *hard, wiry*, and *small*. It was said to be associated with inflammatory affections such as *endocarditis*, or *inflammations of serous membranes*. It is specially a feature of the stage of rigor. It is also manifest after *division of the pneumogastrics* (Sanderson).

The different forms of pulse due to **irregularity of the heart's beat** have already been described under "Functional Diseases of the Heart" (Sect. 497). It should be remembered in this connection, that every heart's beat does not necessarily induce an arterial pulsation. There may be two beats of the heart to one of the pulse.

RAPIDITY IN DISEASE.

The rapidity of the pulse can be influenced by so many collateral and extraneous circumstances, that no very precise rules can be formulated which will hold good in all cases.

It may be said, however, that, generally speaking, it is **increased in rapidity** when there is any degree of acute *fever*, in many *functional diseases of the heart*, and in some *organic diseases of that organ;* while, on the other hand, it is found to be **slower than usual** in the *later stages of fever*, in *some functional diseases of the heart*, in many *nervous diseases where the vagus is stimulated*, in *compression lesions of the brain*, and in *some organic diseases of the heart fibre*—as where it becomes fatty.

The pulse is quickest at the time of birth (135-140 per minute), and decreases with regularity towards old age (75 to 80).

The Sphygmograph.

608. The only accurate means of recording the pulse is by means of the sphygmograph. Space will not allow of a description of the various forms of sphygmograph, and this is rendered the less necessary as nearly every text-book of Physiology contains an elaborate account of them.[1]

The one probably most in use in this country at the present time is Dudgeon's (see his treatise).

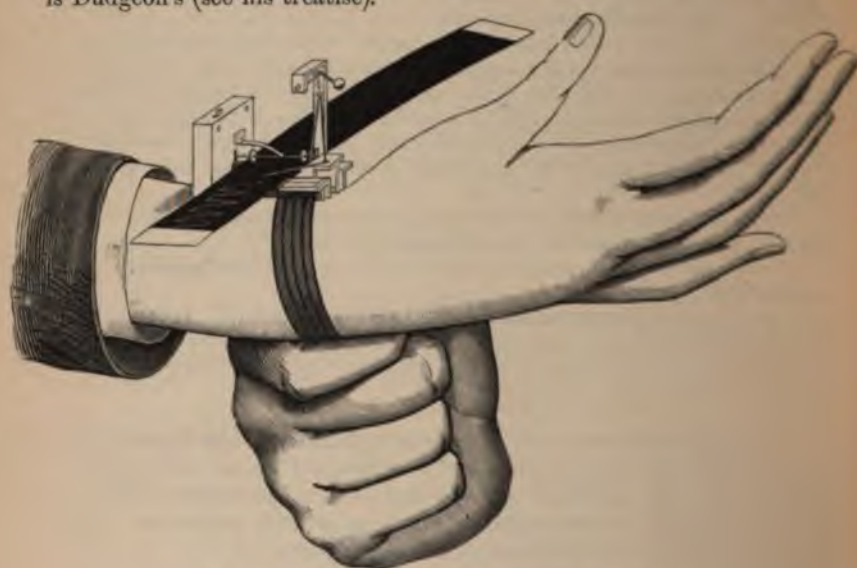

Fig. 210.—Dudgeon's Sphygmograph applied to Radial.

Sanderson (No. 343), a good many years since, pointed out what is now pretty generally recognised, namely, that the sphygmograph cannot be relied upon alone as a means of diagnosis of any particular disease. Its uses in disease, he asserts, are to indicate the mode and direction of the contraction of the heart, the soundness of the arteries, and the relative amount of blood contained in the veins, that is to say, the balance of pressure between venous and arterial systems.

It must be remembered that the tracing may differ on the two sides, and that it is often widely divergent in various individuals suffering from the same disease.

The Normal Sphygmogram.

Fig. 211 will serve to show the several parts of the normal sphygmogram of the radial artery.

[1] For a concise statement of the various forms of sphygmograph which have been in use from time to time, the reader is referred to Dudgeon's excellent little treatise on "The Sphygmograph." See also Bibliography.

It is characterised by a vertical **percussion** or **up-stroke** (*a*) corresponding to the primary pulse wave propagated from the contracting ventricle. It is usually perpendicular in health, and has a pointed apex.

Its greater or less amplitude indicates a corresponding amount of distensibility of the artery. It is fuller where the artery has freely discharged its blood before the pulse wave has been liberated, and hence is indicative of a relaxation of the coats and low tension. It is particularly high where a powerful pulse wave is propagated into a relaxed artery, as in some cases of hypertrophy of the left ventricle.

From the apex, the tracing descends (*c*), and terminates in a small elevation (*d*). This elevation (*d*) is known as the **tidal** or **predicrotic wave.**

In a schema composed of a series of tubes containing fluid the greater the inertia of the fluid the more marked this elevation becomes. It almost vanishes when the tubes contain air, and is greatest when they contain mercury (Marey).

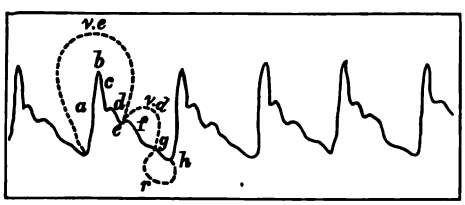

FIG. 211.—NORMAL SPHYGMOGRAM (MODIFIED FROM DUDGEON). PRESSURE 2 OZ.

(*a*) Vertical upward stroke (systolic or percussion wave or stroke); (*b*) apex of up-stroke; (*c*) a downward stroke of varying length; (*d*) a curve called the first tidal, or predicrotic wave; (*e*) an angle called the aortic notch; (*f*) a second curve called the aortic curve, or dicrotic wave; (*g*) a slight curve called the second tidal wave; (*h*) termination of downward stroke; (*v.e.*) the dotted line corresponds to period of systolic contraction; (*v.d.*) to that of ventricular diastole; (*r*) to that of period of rest before commencement of systole.

The predicrotic elevation is succeeded by a larger notch (*e*) usually known as the **aortic notch,** and this is followed by a second elevation (*f*). This second elevation is named the aortic curve or **dicrotic wave.** Numerous as have been the theories as to its causation, opinion is now pretty well made up in favour of the explanation originally offered by Garrod (No. 149, xix. 1871, p. 322). It is as follows :—

The notch (*e*) corresponds in time to the closure of the aortic valve, and at that time, of course, the blood recoils against the cusps from the elasticity of the arterial walls and from that of the tissues. This causes a wave to be reflected from the valve which is propagated into the arteries, and causes the lever of the sphygmograph to be slightly raised, and thus to inscribe the elevation *f*.

In support of this view, it is now recognised that when the aortic valve is destroyed by disease, the dicrotic wave is either absent or small, probably in proportion to the extent of the injury to the cusps.

Marey (No. 346, p. 719) has constructed a model in which he imitates the conditions present in the natural state of the parts, and when the aortic valve is deficient.

It represents the heart with its valves, and the arterial, venous, and capillary systems. By an ingenious arrangement, he can induce different degrees of incompetence of the aortic orifice, whereupon it is noticed that the tracing taken by means of a sphygmograph entirely loses the dicrotic wave.

The same thing happens when a sound is introduced through the carotid of an animal down to the aortic orifice, and the valve destroyed by means of it, as illustrated in the accompanying figure.

The fact also that it becomes smaller the further the artery is removed from the heart, lends additional support to this view.

At the point *g* there is often a second elevation similar to *d*, but smaller. It is supposed, like that at *d*, to be due to *oscillation*. The part of the down-tracing from *g* to *h* indicates the period of rest in anticipation of the ventricular contraction.

The lowest point of the up-stroke has been termed the **base line** by Landois (No. 348, p. 81). Mahomed (No. 350, i. p. 71) calls it the **respiratory line**, because it varies in height with inspiration and expiration.

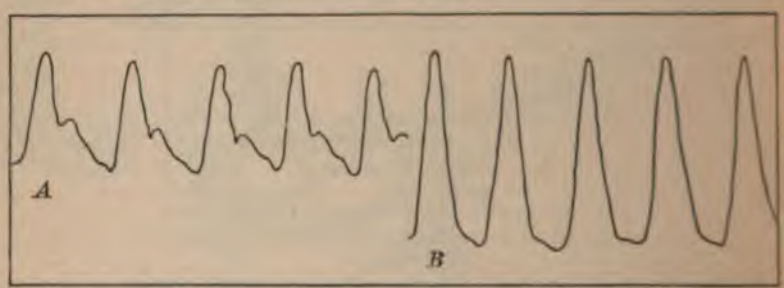

FIG. 212.—MODIFICATION OF THE TRACING IN FACIAL ARTERY OF HORSE AFTER DESTRUCTION OF AORTIC VALVE.
A, before, B, after production of insufficiency.

The line of descent may be more or less gradual. Where the blood passes easily out of the peripheral vessels, as where the arterioles are relaxed, it becomes more and more vertical, but where there is obstruction to the free outflow of the arterial blood, as in Bright's disease, it is prolonged.

The descent stroke may sink so low in some cases, that it passes below the base line. According to Dudgeon (No. 345, p. 42) this is seen in young persons, in those who are under the influence of alcohol, in the dicrotic pulse of chlorosis, in typhoid, and in hectic states of the body.

On the other hand, it may form a mere notch at the apex of the percussion stroke. This indicates a condition of feeble contractility of the arteries, such as occurs in old persons (Dudgeon).

Corresponding Stages of Heart's Rhythm.—These are diagrammatically shown in Fig. 211. The dotted line *v.c.* is contemporaneous with the ventricular systole; that represented by *v.d.* cor-

responds to the ventricular diastole; while *r* represents the period of rest before the commencement of the systole.

SIGNIFICANCE OF THE TIDAL WAVE.

This has been explained more philosophically, and put more tersely by Mahomed than by almost any other writer.

He said: "The simplest pulsatile movement that can be conceived in an elastic tube is the mere passage of a wave of fluid through it, causing more or less sudden expansion and a gradual collapse of the tube, as it passes through it; such a wave is the foundation of the pulse, and has been called the 'Tidal' wave (Fig. 212 α).

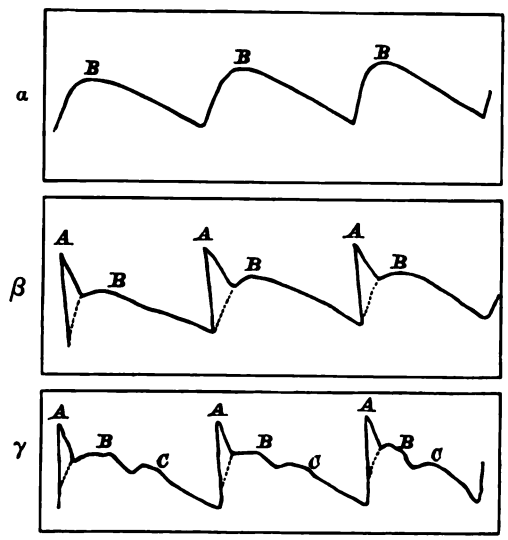

FIG. 213.—MAHOMED'S SCHEME OF TIDAL WAVE.

If the impulse imparted to the fluid is more sudden, an element of percussion or shock will be introduced (Fig. 212 β), giving an abrupt and verticle up-stroke, from the jerking up of the lever by the sudden expansion of the artery. Owing to its acquired velocity, this movement of the lever is rather greater than the corresponding movement in the arterial wall which produced it, and on reaching its highest point it falls suddenly by its own weight, till it is again caught and perhaps slightly raised by the tidal wave B, which is now only reaching its maximum of distension. . . . The tidal wave is the true pulse wave, and indicates the passage of a volume of blood through the arteries, pumped into them by each contraction of the heart. It resembles the passage of the tidal wave or 'bore' up a river; hence its name. It is transmitted more slowly than the percussion wave, or rather attains its maximum intensity more gradually; hence their separation in the tracing. Though they usually commence to distend the artery together, the percussion wave necessarily attains its maximum intensity instantaneously, it being only a shock, while the tidal wave does so more gradually. Sometimes a considerable interval elapses be-

tween them. Frequently they are inseparable, the percussion wave not existing or else being merged into the tidal."

This, however, is not the invariable view taken of the cause of the tidal wave. Dudgeon, for instance, regards it as rather the effect of oscillation set up by the inertia of the liquid. It is said to be increased in extent when a large volume of blood is discharged into the arteries, as from a dilated heart (Bramwell).

Literature on the Pulse and Sphygmograph.—**v. Basch**: Berl. klin. Wochnschr., xxiv. 1887, p. 179; *Ibid.*, p. 987. **Bramwell**: Student's Guide to the Examination of the Pulse, 1883. **Broadbent**: Brit. Med. Journ., 1887, i. pp. 655, 707, 761. **Chapman**: Brit. Med. Journ., 1882, ii. p. 297. **Dudgeon**: The Sphygmograph, 1882. **Foster (B. W.)**: The Sphygmograph in the Investigation of Disease, 1866. **Foster (M.)**: A Text Book of Physiology. **Galabin**: Journ. Anat. and Phys., x. 1876, p. 297. **Landois**: Die Lehre vom Arterienpuls, 1872. **Mahomed** (Sphygmograph) Gant's Science and Practice of Surgery, i. 1886, p. 67; Trans. Path. Soc., xxvii. 1876-77, p. 394; Med. Times and Gaz., 1872, ii. p. 143: Guy's Hosp. Rep., xxiv. 1879, p. 363. **Marey** (Sphygmograph): Journ. d. la Physiol., iii. 1860, p. 241; Physiologie méd. de la circul. du sang, 1863; Du mouvem. dans les fonct. de la vie, 1868, p. 156. **Moens**: Die Pulscurve, 1878. **Sanderson**: Handbook of the Sphygmograph, 1867. **Vierordt**: Die Lehre vom Arterienpuls u. s. w., 1855.

Means of Artificially Modifying the Arterial Pressure.

609. When any one or more of the factors above enumerated at page 694 as instrumental in keeping up the pressure within the arteries becomes modified, it will react upon the tension of the vessel unless compensated for in some way.

The mean pressure of the blood within the arteries, as is well known, **may be raised** by various physiological expedients, as by *stimulating the vaso-motor centre in the medulla, compressing large arterial trunks* such as the femorals or the aorta, applying *cold* to the surface of the body, or by interrupting *the blood supply to the brain* through the carotids.

Application of *warmth* to the surface of the body, as by the warm bath, has the effect of relaxing the arteries and **lowering their tension.** The manner in which cold and heat thus oppose each other is worthy of further investigation. Does cold affect the arterioles directly and solely? Or is there an equivalent tonic contraction of the whole musculature of the body, rendering the difficulty of circulation through the muscles greater, and thus raising the pressure? Does heat influence the muscles in an opposite direction, rendering them more lax, and so aiding the facility with which the blood will circulate through them?

The arterial pressure is also lowered by *stimulation* of the *depressor nerve, venesection*, the *inhalation of nitrite of amyl*, etc. In all these cases, the arterial channels are rendered relatively or actually wider so as to accommodate more blood. *Division of the cervical cord* in the rabbit similarly lowers the arterial pressure by inducing a relaxation of the muscular coat of the arterioles, hence rendering the passage of the blood into the capillaries easier. *Excessively high temperature*, where artificially applied to an animal, causes a lowering of the arterial pressure by a paralysis of the heart (Paschutin).

The heart's beat and the arterial pressure are so far mutually dependent, that when the pressure within the arteries rises beyond a

certain mean level, the rapidity of the former decreases, and thus allows time for the arteries to discharge their superfluous blood before the next systole.

Where it happens, as in some forms of disease, that this compensatory regulation of the heart proves ineffectual in lowering the arterial pressure, the heart will be found labouring against it. The impulse is long and heaving, and so great may the arterial tension be, that a shock is felt during diastole from the impact of the arterial blood against the aortic valve.

Diseases Accompanied by High Arterial Pressure.

610. In some individuals, a high arterial pressure seems to be a **natural phenomenon.** Mahomed (No. 63, xxiv. 1879, p. 379) declared that this persistently high pressure is hereditary, and is one of the chief predisposing causes of chronic Bright's disease. It is present in the young, and may be long manifest before the kidney disease makes its appearance. He went so far even as to say that an individual with a permanently high arterial pressure may, practically speaking, be said to have chronic Bright's disease either with or without structural changes of the kidney (*loc. cit.*, p. 387). He also stated that high arterial pressure becomes more evident with **old age.**

The usual diseases which are associated with a high arterial pressure pulse are the various forms of **nephritis,** with the exception of those resulting in suppuration. It is found in **gout** and in **lead poisoning,** but as these diseases are usually accompanied by cirrhotic disease of the kidney, it is possible that this may account for it. The other view of course is tenable, namely, that the cirrhosis of the kidney is due to the prolonged high arterial pressure. The former, however, is most likely correct. Marey (No. 346, p. 190) states, that, when the renal arteries are compressed in the cat, the pressure within the carotid shows a notable rise.

In certain forms of **anæmia,** the pressure, according to Mahomed and Broadbent, is persistently high. This, however, does not hold good for all cases. It is probably in those where the blood is of very poor quality that the arterial tension is highest. Such blood circulates through the capillaries with difficulty, and hence tends to retard the outflow from the small arteries.

In **peritonitis,** in various diseases of the lung such as **emphysema, chronic bronchitis,** and **acute pneumonia,** and in **pregnancy,** the arterial pressure is also abnormally high.

It must not be concluded, however, that, because it is high in these diseases, as a rule, it will be found to be so always. Each case has its own special idiosyncrasies and must be studied accordingly. The only certain means of determining the arterial pressure is by measuring it, a procedure of primary importance in therapeutics.

The Pulse.—As the blood is driven from the heart into arteries

already tense from peripheral resistance, the pulse should be one in which the percussion stroke is not well felt. In some diseases it is small (peritonitis), in others it is large (chronic Bright's disease). The difference depends on whether the heart is able to cope with the arterial resistance. In peritonitis, the heart's action is depressed; in chronic Bright's disease it is vigorous, the wall of the left ventricle being hypertrophied. The condition of high pressure also renders the heart's action slower, hence the down part of the sphygmographic curve is correspondingly long.

Fig. 214 from Mahomed gives the tracing of the pulse of a person who probably suffered from incipient chronic Bright's disease, and in whom the arterial pressure was abnormally high. It will be noticed that the up-stroke is comparatively short, the tidal wave is high, but the dicrotic wave is low, and the down stroke between the aortic wave and the base line is long.

The mere feeling imparted to the finger is deceptive, for a pulse of high tension may be either large or small. The high tension may be associated with an exhausted heart, and hence the pulse may be

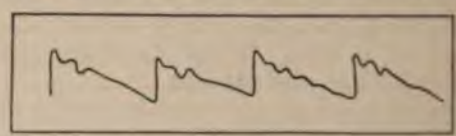

FIG. 214.—PULSE OF HIGH TENSION; INCIPIENT BRIGHT'S DISEASE.

small, a condition which, as Mahomed (No. 63, xxiv. 1879, p. 372) rightly remarked, is usually thought to require stimulation, but which, in reality, is much benefited by depletion. Of all the characters of a high pressure pulse, according to the same authority, the least constant is that of *hardness* and *incompressibility*. Many pulses of high tension certainly possess this character, but not all. A pulse of undue length and of a pushing character is a more reliable indication.

It is long, persistent, and hard. It is the *pulsus tardus* or "long pulse" of the older physicians, the expression of a heart labouring against undue resistance.

Bramwell (No. 349, p. 50) and others differ from Mahomed in reference to hardness or incompressibility not being a reliable guide to the recognition of a high-pressure pulse. It certainly might be supposed, if an artery were in an unusually tense condition, that it should feel hard and incompressible. Probably the chief source of error lies in the supposition that a hard pulse is always one of high pressure, whereas an artery may be so hard as to be diagnosed as calcareous during life, and the hardness be simply due to an unusual thickness of the coats. It might with more truth be said that a hard incompressible pulse *in a previously healthy individual* indicates high pressure. Such a pulse is commonly met with in acute inflammations.

Methods of Gauging.—Mahomed (No. 63, xxiv. 1879, p. 371) was in the habit of gauging high pressure by drawing a line from the

apex of the up-stroke to the deepest part of the aortic notch (Fig. 215 AB). No part of the tracing should rise above this; if it does so, the pulse is one of high pressure.

The *height of the aortic notch* has also been regarded (Landois, No. 348, p. 81) as another good means of gauging. The nearer it approaches the base line the lower the pressure is (Fig. 215 BC).

Occasionally, the systole of the ventricle with a pulse of high pressure may be prolonged. Thurston (No. 185, 1881, i. p. 455) estimates this prolongation by measuring the length of the interval between the commencement of the ascending stroke and the aortic notch, and comparing it with a normal pulse tracing of the same rapidity. Regarding, as he does, the aortic notch as the termination of the systole, he looks upon its position as an important indication of the prolongation of the ventricular contraction; or, in other words, of the impairment of the muscular tissue of the ventricle.

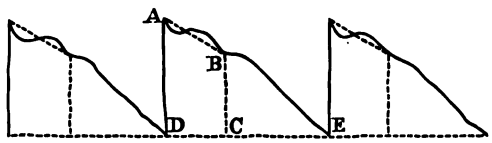

FIG. 215.—ILLUSTRATION OF MAHOMED'S METHOD OF GAUGING ARTERIAL PRESSURE.

ILL EFFECTS OF PROLONGED HIGH ARTERIAL TENSION.

The tension of the arteries tends to predispose to **apoplexy,** especially cerebral apoplexy. Where it is continuous, it seems to be one of the most powerful predisposing causes of chronic **Bright's disease,** or, at any rate, the two conditions are intimately associated. It constitutes a most important element in **pneumonia.** When long continued, it will lead to **hypertrophy** or to **dilatation of the left ventricle,** or to both combined. It modifies the whole of the vital processes, and hence its timely diagnosis is of the greatest moment.

REDUCTION OF HIGH ARTERIAL PRESSURE.

The most ready means undoubtedly is to be found in venesection. Hales was the first to recognise that, as the blood flows, the pressure falls and the pulsations of the heart increase in frequency. Modern physicians are beginning again to recognise this fact.[1]

The effect of moderate hæmorrhage is to amplify the pulse waves, so that the sphygmogram becomes dicrotic. Thus in Fig. 216 is represented the tracing from a radial pulse before hæmorrhage, while in Fig. 217 is shown the tracing of the same pulse after hæmorrhage.

[1] The reader is specially referred to Broadbent's excellent lectures on the pulse for a clear statement of the beneficial effects to be derived from venesection (*British Med. J.*, 1887, i. pp. 655, 707, 763). See also preceding remarks. Section 364.

In Fig. 218 are represented the sphygmograms from the carotid of a horse, from which Marey and Chauveau (No. 346, p. 337) abstracted varying quantities of blood. Line 1 represents the tracing before any blood had been abstracted; line 2 shows the condition of the pulse when the animal was lying down—of less amplitude than in the former; line 3, five litres of blood were abstracted; line 4, another depletion to five litres; line 5, depletion to two litres; line 6, further depletion to two litres; line 7, still further depletion to two litres.

After each hæmorrhage, there was an increase in the frequency of the pulse, which rose from 45, to 108 beats per minute; and at each acceleration it exhibited the characters of feeble tension. The blood

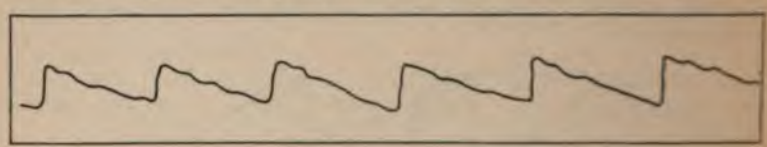

FIG. 216.—RADIAL PULSE BEFORE HÆMORRHAGE.

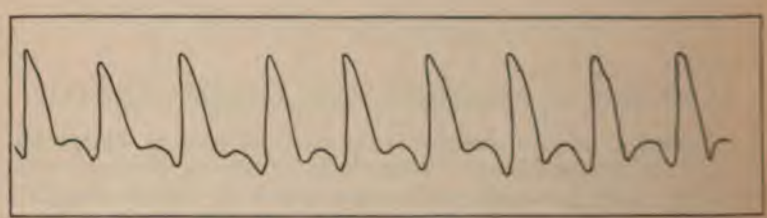

FIG. 217.—RADIAL PULSE AFTER AN ABUNDANT HÆMORRHAGE IN SAME SUBJECT.

propelled into the vessel from the heart, or as it recoiled from the aortic cusps, met with feeble resistance, and, hence, gave rise to the characters of dicrotism. The pressure at the end of the experiment had fallen from 15 to $5\frac{1}{2}$ cm. of mercury.

Similar effects follow depletion in Man.

If, however, the hæmorrhage be very copious, Marey states (No. 346, p. 290) that the vessels begin to contract, and so render their calibre narrower, with the effect that the ample pulse waves again disappear.

DISEASES ACCOMPANIED BY LOW ARTERIAL PRESSURE.

611. It may happen that the natural resilience of the arterial walls is lost through their having become diseased. Atheroma is usually quoted as the commonest cause of this. It is possible, however, that the low arterial pressure co-existent with it, may, in part, be accounted

for by the enfeeblement of the heart which so often accompanies an atheromatous state of the arteries, or by loss of elasticity in the tissues generally throughout the body.

The diseases with which a low arterial pressure is associated are

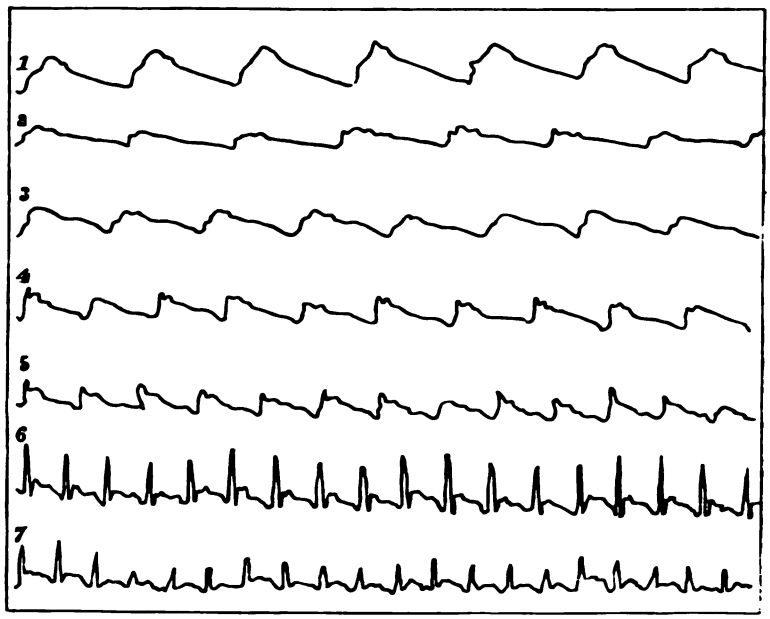

FIG. 218.—TRACINGS FROM THE CAROTID OF A HORSE AFTER REPEATED VENESECTIONS.

chiefly certain **valvular lesions of the heart,** diseases accompanied by **great prostration,** certain, although not all, cases of **anæmia, fevers, collapse,** etc.; but in this, as in the opposite condition, no certain rule can be laid down.

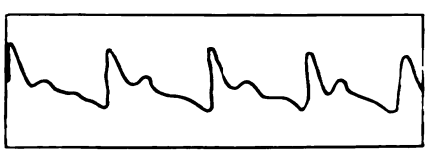

FIG. 219.—LOW TENSION PULSE OF PATIENT FROM WHOM FIG. 214 WAS OBTAINED—AFTER TREATMENT.

Pulse of Low Pressure—Dicrotic Pulse.—Fig. 219 shows a tracing from the pulse of the same patient from whom Fig. 214 was obtained, after being subjected to careful treatment. It is now the sphygmogram of a pulse of low tension. The up-stroke is le than previously, and its apex is less pointed; the tidal wa

almost disappeared; the aortic notch is deep; and the dicrotic wave is high; while a post dicrotic wave is recognisable in all the curves.

Various degrees of dicrotism are recognised, which the accompanying three figures from Mahomed may serve to illustrate.

The degree of dicrotism is calculated from the relative position of the aortic notch to the base line. If, as in A, it is simply more indented than usual, it is known as **dicrotic.** If the notch is on a level with the base line, it is called **fully dicrotic** (B); and if it is actually

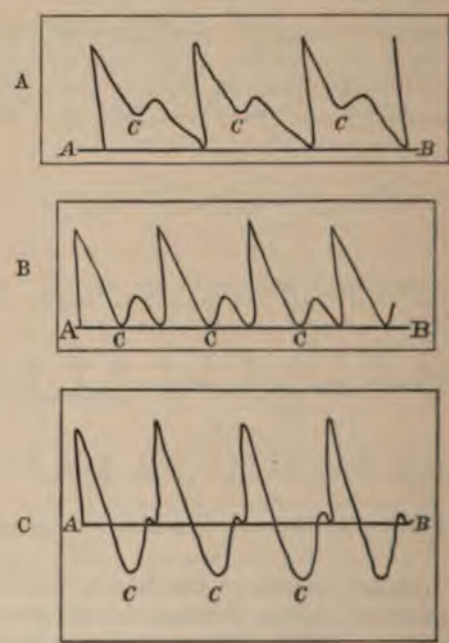

FIG. 220.—SCHEME OF DIFFERENT DEGREES OF DICROTISM.
A, slightly dicrotic. B, fully dicrotic. C, hyperdicrotic.

below the base line, as sometimes happens, it is said to be **hyperdicrotic** (C).

The cause of the dicrotic pulse is simply that the small arteries and capillaries are in a state of relaxation, and allow the blood to pass readily through them. The natural elasticity of the vessel then comes into play, and the walls tend to collapse. This allows the lever of the sphygmograph to sink, hence the depth of the aortic notch.

The term dicrotic was applied to this pulse long before the invention of the sphygmograph, simply on account of a double stroke being felt in the arteries with each cardiac systole. It is often an indication of feeble vascular tone due to paresis of the vaso-constrictor nerves, and is a frequent accompaniment of fever with prostration.

The dicrotic pulse must not be mistaken for the pulsus bigeminus (see p. 574), where the beats run in couples, but where they are each due to a cardiac systole. The pulsus bigeminus is due to irregularity in the heart's action.

In regard to the *feeling* imparted to the finger by a pulse of low pressure, Broadbent (No. 6, 1887, i. p. 710) states, that the one unequivocal sign is the absence of all resistance in the artery between the beats. The impulse is also usually great, owing to the relaxed state of the vessels permitting of a copious pulse wave.

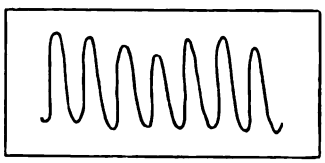

FIG. 221.—MONOCROTIC PULSE.

Monocrotic Pulse.—The dicrotic wave may be entirely absent. Such a pulse is designated **monocrotic.** It is usually increased in rapidity. It is a sign of very low tension, the recoil wave not being sufficiently powerful to be reflected from the aortic valve.

The pulse of *fever* is sometimes of this type. The arterial tension is not only low, but the tissues are relaxed, while the heart is contracting vigorously and with increased rapidity. Hence the pulse has a particularly full character, each heart's systole impelling a voluminous wave along the relaxed vessels. As collapse approaches, the heart's action being less vigorous, the pulse may become both small and compressible.

TRICROTIC PULSE.

612. A tricrotic wave may sometimes be added to the tracing. It is supposed to be simply an exaggeration of the oscillatory wave which sometimes follows the dicrotic in the normal sphygmogram.

According to Landois (No. 348, p. 80), the up-stroke may also be sometimes marked by a series of small waves. It is questionable whether they may not be due simply to vibration of a defective lever. He designates the curve as **anacrotic** when the ascending part is interrupted by a number of smaller elevations; and as **catacrotic** when the descending part is similarly intersected. According to the number of these smaller curves, he employs the terms **anadicrotic, anatricrotic—catadicrotic, catatricrotic.**

PULSE IN VALVULAR DISEASE OF HEART.

613. Most writers who have given much attention to the subject, are agreed that the tracings to be derived from the arteries in valvular disease cannot be relied upon as of much diagnostic value. They vary even with what might be regarded as an identical lesion of a particular valve in different individuals. This is only to be expected, seeing that the amount of injury to the orifices, and the condition of the cavities and walls of the heart, seldom correspond in any two cases.

Aortic Regurgitation.—Of all the pulses connected with valvular disease, this is said to be the most characteristic. Corrigan described it as something *sui generis* (Corrigan's pulse). It is distinguished by a rapid and full impulse, falling off almost immediately afterwards

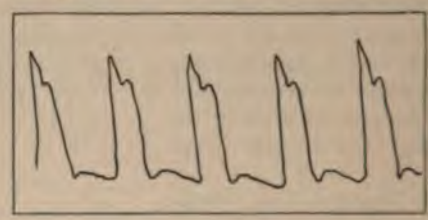

FIG. 222.—CORRIGAN'S PULSE.

owing to the reflux of the blood through the incompetent aortic valve. It has sometimes a vibratile feeling, like that of the toy known as a water hammer, so that the terms "water-hammer-pulse" or "splash-pulse" is often applied to it.

The heart usually contracts vigorously in this disease, hence the

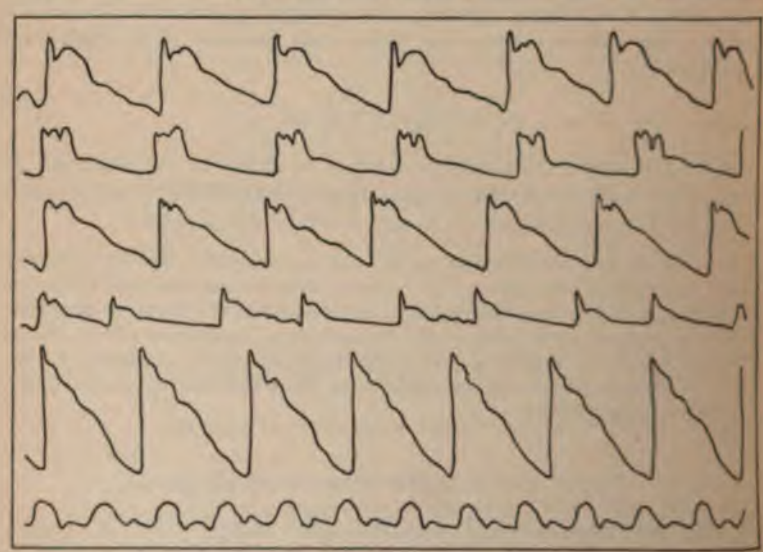

FIG. 223.—TRACINGS OF RADIAL PULSE IN AORTIC ANEURISM.

up-stroke is perpendicular. The aortic insufficiency also diminishes the intensity of the dicrotism by there being only an impaired aortic valve to reflect from, or owing to its being entirely destroyed. The dicrotic wave consequently becomes less and less pronounced, the

greater the extent of the destruction. Fig. 222 may be taken as a good sample of the tracing from this pulse.

In other forms of heart disease tracings cannot be relied upon as of constancy. They often closely resemble tracings in which no valvular disease exists.

Pulse in Aneurism.

614. Where an aneurism is placed upon the course of a large artery, it usually modifies the sphygmogram. If the aneurism be thoracic, or if it be located upon any part of an artery of the trunk leading to the upper extremity, the two radials may show different tracings. Bramwell says (No. 349) that the apex of the tracing may become blunted where the blood passes through the sac. There is,

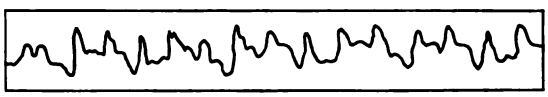

Fig. 224.—Tracing of the Pulse in Asthma.

Fig. 225.—Sphygmogram of Pulse of an Old Person—Female.

however, no sphygmogram which may be said to be characteristic. The accompanying tracings by Marey (Fig. 223) will give some idea of the variety of forms that may be met with in thoracic aneurism. The fact of there being a difference in the two sides, would, when taken along with other physical signs, be more indicative of the disease than any peculiarity in the tracing itself.

Pulse under Various other Conditions.

615. **Atheromatous Arteriitis.**—The tracings in this disease are very uncertain, and depend greatly upon its situation and extent. Arteries are so frequently diagnosed as atheromatous, which do not show after death the slightest trace of the disease, that little reliance should be placed upon statements regarding the pulse, which have not been confirmed by *post-mortem* examination.

In Asthma.—The tracing in an attack of asthma may show a very irregular base line, owing to the spasmodic character of the breathing. The accompanying figure from Dudgeon demonstrates this.

Old Age.—The characters of the tracing of the pulse in an old person, in whom the arteries generally lose some of their elasticity, are the following (Marey, No. 346, p. 620): (1) Its amplitude is great; (2) the line of ascension is brusque, sometimes jerky; (3) the summit of the pulsation forms a plateau; (4) the curve falls brusquely after the systolic plateau; (5) the line of descent is generally devoid of dicrotism.

The amplitude is accounted for chiefly by the dilatation and loss of elasticity of the vessels. The loss of the dicrotic curve is owing to the same cause. A certain elasticity of the arteries is necessary in order to enable the blood to recoil from the aortic valve.

In Maniacs.—Consult *Ziehen: Sphygmographische Untersuchungen an Geisteskranken.*

APPENDIX

Making of Casts, Models, etc.

A most important element in a pathological museum is a series of well-executed casts and models, and as those which can be procured ready-made on the Continent and elsewhere, illustrative of morbid anatomy, are so unlike what they are intended to represent as to be almost useless, a few general directions on this branch of technology may not be amiss.

For several years the author has employed rough models in combination with drawings to great advantage in teaching. They should be of such size as to be readily seen from all parts of a large lecture room. French and German models are as a rule too small, and in many cases too intricate.

Casts of morbid organs are much preferable to any drawing that can be made, and as they are just as easily, or more easily executed, there is no reason why they should not in part be substituted for them. An intelligent mechanic can be readily trained to the work, provided that the colouring is carefully superintended by the pathologist himself. It is here that most casts fail; their colouring is artificial, and often, not copied from nature.

For the making of casts (not mere models) the use of two substances is to be recommended, namely, plaster of Paris, and what the author proposes to call after its inventor, "Cathcartine." The latter is superior to wax, plaster, or any composite. The absolute truthfulness of the minute impressions, the lustre, and, what is still more remarkable, the pliability of this substance, place it far above any other mixture for all pathological objects.

The Plaster Cast.—Many casts are made of ordinary plaster coloured with oils, and, certainly, for some organs it suits very well. Liver, lung, and kidney show admirably when cast in this.

(*a*) *Making of the Mould from a Clay Model.*—Two methods may be adopted in making the mould. It may either be taken directly from the subject in gelatine or "Cathcartine," or the subject may first be modelled in clay, and the mould subsequently taken from this. Where the subject is of a very delicate nature and would be injured by making a mould directly from it, model it first in clay. The unhardened brain, the eye, and other delicate organs must be treated in this way. It is always preferable, of course, to mould from the organ itself.

Modelling in clay is very easy as compared with limning on paper or canvas. The kind of clay to use is either pipe-clay, or, what is even preferable, a fine red

clay which is sometimes to be procured, and which is much cheaper. The modelling is in great part done with the thumb, aided by certain tools to be procured from any artist's colourman. All measurements should be carefully taken with calipers and compasses. The model being finished, the surface is allowed to get slightly dry by exposure. When it has become firm, it is coated over with spirit varnish which is allowed to evaporate. If the subject is a round one in which it is necessary to show all sides, two stout iron wires should have been run through the clay; in fact the model ought to be moulded upon these. They serve as supports when the outer plaster casing is adjusted.

The next stage consists in making *the outer plaster casing*. The clay model is loosely covered with strips of thin dry paper, care being taken of course not to injure it by so doing. Slabs of clay about a quarter of an inch thick are to be rolled out on a flat surface, and long strips cut from these are now laid over the paper. At the points where the strips of clay meet, the intervals are to be closed with additional pieces of clay, and with the thumb the whole is to be made into a uniform conical shape. Plaster of Paris is next run over the clay in a layer from half to one inch thick, and is allowed to set. If it is a round subject, such as a brain, this plaster covering is to be built up in halves, the lower one first, bringing the wires out between them. When the lower half of the casing has begun to set, the surface which is to be in contact with the upper half, is to be smoothed down; and when quite hard it must be coated with some substance which will prevent the two from adhering. The best mixture for the purpose is composed of stearin, liquid paraffin, and a little gum dammar, so thick that, when cool, it has the consistence of honey. It is melted on a warm bath, and it may be rubbed on cold with a hog's hair brush. In order that the two halves of the casing may come into accurate contact when adjusted round the subject, it is necessary to fix them securely by means of a peg at each end which fits into a corresponding hole. This is easily done when making the lower half. A conical-shaped hole is bored in its surface of contact, and is smeared with the stearin mixture. In making the upper half the plaster runs into this and forms of course an accurately fitting peg. The upper half of the casing is made in the same manner as the lower. When both have thoroughly set, they are separated, and the clay and paper are removed from the surface of the subject. A hole is next bored at one point in the casing through which the material employed in making the mould may be poured. The subject is replaced within the casing supported of course by the wires at each end. The join in the two halves of the casing is rendered water-tight by clay, and the whole casing is bound together with stout cord to prevent the upper half floating up from the lower when the material used for the mould is poured in.

All is now ready for making the mould, and it next comes to be a question of what it is to be composed. That which is generally employed is a very strong solution of gelatine. The gelatine ought to be soaked in water until quite pliable, and melted in a water-bath. A little carbolic acid may be added for preservative purposes, mixed up with some glycerine. The solution must be so strong that when cool it can be pulled about like a piece of indiarubber, and hence, of course, must contain simply enough water to melt it. A material which is superior in many respects is the before mentioned "Cathcartine," the composition of which is described thus by Dr. Cathcart, its inventor (No 19, Nov. 1885, under *Trans. of Edin. Med.-Chirurg. Soc.*).

Soak glue, or what is preferable, ordinary French gelatine, in water until it has been thoroughly softened. Allow it to lie exposed so that the water may evaporate to such an extent that the gelatine becomes pliable but not soft. Melt this in a water-bath, and add to it as much glycerine by measure as there was dry gelatine by weight. It is also advantageous to add to the glycerine about 1 to 40

carbolic acid. Mix them thoroughly, and stir in the finest ground oxide of zinc suspended in a little glycerine until the whole mass assumes an opaque white appearance.

This material is invaluable for making either a mould or a cast. For the former it is preferable to pure gelatine on account of the impression being finer.

When the space between the outer plaster casing and the subject is nearly filled with the medium employed in making the mould, the casing is moved about so as to allow any retained air to escape. It is then completely filled up to the margin of the aperture and allowed to stand for a night, so that the mould may thoroughly solidify. The casing is taken off next morning and the mould cut round into halves with an ordinary scalpel, a piece of about one inch being, however, left to act as a hinge. The subject is removed, and a hole is made in the mould at one part (the least important and flattest) through which plaster may be poured. The interior is smeared with oil, the halves readjusted, and the mould is again placed inside the plaster casing, the two parts of the latter being held together with strong twine. If the aperture in the mould does not correspond with that in the casing, make a fresh one in the latter. The plaster employed for the cast should be freshly roasted, and be of the thickness of rich cream. It is poured into the mould through the aperture and allowed to run first over the least intricate part. The casing is now rolled about in such a manner that the plaster runs into every crevice, and when the interior has received a thorough coating the waste plaster is allowed to escape. A second lot of plaster *less in quantity than the first* is prepared, and when the first coating has set, this is poured in and moved about as before. Place the ball of the thumb over the aperture just as the plaster is beginning to thicken, and use this as a plug, so that the aperture itself may become filled up. As soon as the second layer of plaster has set, remove the cast from the mould, and make another or several others. Keep one as the permanent subject from which again to throw off duplicates, should they be required. The gelatine or "Cathcartine" of course may be melted for another cast. If the subject be spherical, as we have supposed, the cast will be hollow, and all that remains to be accomplished is to cut off the piece of plaster which filled the opening in the mould. That is easily done with a knife or by modelling instruments for the purpose.

B. *Making the Mould from the Actual Subject.*—Where the gelatine mould is made from the organ directly, the latter should be pinned down upon a board to prevent it floating. A wall of clay is next to be built up about three-quarters of an inch all round it, and into the chamber so enclosed is to be poured the melted gelatine or "Cathcartine." The organ can be easily removed when the mould is cool. The plaster is now run into it as before.

Painting the Plaster Cast.—Plaster casts ought to be painted with a mixture of oil paint, turpentine, and gold size. The plaster must be allowed to become thoroughly dry before being painted. It is best to dry it in a warm room or before a fire, and while still warm and perfectly free from moisture, its surface is to be coated with boiled linseed oil. After this has soaked into it, the cast is ready for painting. The organ from which it was taken should meanwhile have been kept in ice or in the glycerine and arsenic mixture described in Section 27. After the paint has thoroughly dried it should be covered with one or two coats of copal varnish.

The Cathcartine Cast.—The mould must be made in plaster and in one piece. This can be easily done without coating the surface of the organ with any lubricating mixture. If it is made in several pieces the seams leave ridges on the cast which cannot be removed. With the majority of organs the mould can be easily confined to one piece, as they are so pliable. Where a surface is hairy it ought to be smeared with a thick soap solution and the hair thus flattened down. It may even be necessary, in the living subject, where the part is extremely hairy, to cover it with a thin wet rag. This readily adjusts itself to the shape of the surface. The mould

having been removed and dried, is coated with spirit varnish. The "Cathcartine" is now poured into it in a melted state and allowed to run all over the interior so as to form a layer about one-quarter inch thick. The mould must be continuously moved about until the medium has set. When thoroughly hardened the cast is pulled out of the mould so as to ensure that every part is loose. It is replaced, and a thin layer of cotton wool is laid over the interior, while over this, again, plaster is poured to the depth of about an inch. The plaster basis, when set, is withdrawn along with the cotton, and followed by the "Cathcartine." The three are finally readjusted, so that the plaster forms a firm support for the cast, and retains it in shape.

Painting the Cathcartine Cast.—Casts made of this material should be painted with a mixture of oil colours, turpentine, and gold size. Where the dull lustre of skin is to be represented the process of "flatting" is to be adopted—that is to say, the paint, which should contain turpentine, is to be touched gently all over with a dry hog's hair brush, so as to remove undue glossiness. A most life-like representation of the lustre of the skin can be produced if a little flour be dusted on with the brush when the paint is half dry, and the excess removed by switching with a piece of light linen or silk rag.

If it be so desired, the paint may finally be covered with a coating of copal varnish, or those parts which are to appear moist can be touched with it.

To make a Mask.—(1) *Where the cast has to be thrown off in plaster* the mould may be made in gelatine if sufficient time can be spared to allow the gelatine to cool. Sometimes, however, this is impracticable, and then the mould must be taken simply in plaster. If a gelatine mould is to be made, the back of the head should be supported on a block of clay, and a wall of clay should be built up of sufficient height all round this to prevent the gelatine from escaping. If it is found necessary to make a plaster mould, the hair ought to be fixed down with the soap solution just referred to, and the face brushed over with clay water or olive oil. Clay water is perhaps the better of the two. The mould should then be built up in pieces, which will afterwards "draw" from the cast—that is to say, which will not be undercut. A thin piece of string may be laid over the subject in a special direction, plaster being continuously applied over this. When the plaster is just becoming hard, the string is pulled upwards, thus severing it at this particular point; or the mould may be taken in one piece and afterwards broken with a chisel and hammer.

(2) *Where the cast has to be thrown off in "Cathcartine,"* of course it does not matter if the mould is made in one piece, and in fact, where practicable, it should always be so. The Cathcartine is so pliable that it will draw out of almost any mould. The mould for a mask and bust can be readily made in plaster in a single piece.

In the making of models the following substances will be found most useful :—

Carton-pierre.—This is an excellent material for making all kinds of *models*, but should be reserved for those which are not to be subjected to very rough usage. The paper model subsequently described will stand more knocking about than one made of this.

Take of paper pulp (dry)	.	3 lbs.
,, flour . .	.	4½ ,,
,, water . .	.	20 pints.
,, glue . .	.	6 lbs.

Precipitated chalk and plaster of Paris, a sufficiency.

The pulp requires to be very fine, and hence it is well to buy it from the paper or picture frame manufacturers, who tear it into very small fragments by means of a special machine. The flour is to be converted into paste with twelve pints of the water, and the remainder of the water is to be used for melting the glue, which

should be first steeped for a night in it. The pulp, paste, and glue are then mixed, and sufficient chalk added to form a thin paste. This is incorporated with plaster of Paris as it is about to be used, a small quantity being rubbed in at a time. A *gelatine mould* is to be employed, and into this the carton-pierre is to be pressed in a thin layer. As the material is heavy, it is advisable not to make the layer thicker than a sixteenth to an eighth of an inch, unless the model be very large. Paint with oils.

Gilder's Putty.—Where a very strong substance is required in constructing a model, gilder's putty may be found useful. It has the following composition :—

Resin	1 lb.
Glue	1 ,,
Boiled linseed oil . . .	2 gills.

Precipitated chalk a sufficiency.

The glue must first be thoroughly soaked in water and melted. The resin is to be dissolved in the boiled linseed oil, and the two are then mixed. They are subsequently stirred into precipitated chalk, so as to make the mixture of putty-like consistence.

Models made of Paper.—Excellent models of large size, where lightness and strength are required, may be made simply of paper and paste. They are chiefly valuable in teaching such subjects as the pathology of the air-vesicles of the lung, the glomerulus of the kidney, the malformations of the genito-urinary organs, and many others that the ingenuity of the teacher may suggest. They give to the student an idea of the relationships of the diseased organ, which otherwise every one engaged in teaching must have found it difficult to impart, and are much preferable to diagrams.

The subject is first to be modelled in clay, and a plaster mould is subsequently taken from this. After drying, stearin is brushed over the inside before a fire, and allowed to soak thoroughly into the plaster. A quantity of coarse gray or brown-coloured paper must be procured, and a large quantity of strong flour paste. If the model is to be large, the paper, or at any rate the interior layers, should be thick, almost like very thin pasteboard ; if it is to be small in dimensions, a thinner paper may be used. The paper is first soaked in water until it becomes quite pliable. A single layer is pressed into the mould, and is covered with paste. A second layer is placed over this and again smeared with the paste, and so on, seven layers being usually sufficient. It should be remembered that the paper is to be *torn*, not cut. The model is now allowed to dry, and in doing so, it will be found that it usually springs spontaneously out of the mould. If not, the mould should be placed with its back before a gentle fire.

The surface of the model is to be covered with a mixture of precipitated chalk and thin gelatine, and when dry, this is rubbed down with a damp cloth. It ought to be painted with a mixture of japanner's gold-size, white lead, and turpentine. When dry, the whole model is to be coated with copal varnish.

If the model is to be made hollow, it may be cast in two halves, these being subsequently united by a torn slip of paper and paste. The interior should be supported by pieces of wood running from side to side.

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